

ANNALS
OF THE
RHEUMATIC
DISEASES



The Official Journal
of the
EMPIRE RHEUMATISM COUNCIL

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THE OFFICIAL JOURNAL OF
THE EMPIRE RHEUMATISM COUNCIL

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CONTENTS

	PAGES
THE RHEUMATIC NODULES IN THE HEART. LUDWIG ASCHOFF, M.D., FREIBURG-IM-BREISGAU.	161-166
A REVIEW OF RECENT ITALIAN WORK ON RHEUMATISM. PAOLO RAVENNA, M.D., TURIN.	167-179
THE FORMOL-GEL REACTION AND ERYTHROCYTE SEDIMENTA- TION RATE IN ACUTE RHEUMATISM. C. A. GREEN, M.B., S. THOMSON, M.B., AND SURGEON- LIEUT. A. J. GLAZEBROOK, R.N.	180-195
RHEUMATIC SUBCUTANEOUS NODULE FORMATION. F. DUDLEY HART, M.B., M.R.C.P.	196-200
THE SOCIOLOGICAL ASPECTS OF THE TREATMENT OF ARTHRITIS. J. J. R. DUTHIE, M.B.	201-209
JUVENILE RHEUMATISM IN LONDON. FRANCIS BACH, D.M., N. GRAY HILL, M.B., T. WARWICK PRESTON, M.D., M.R.C.P., AND C. E. THORNTON, M.B.	210-241
ABSTRACTS AND REVIEWS OF CURRENT LITERATURE.	242-245
QUARTERLY REPORT OF THE EMPIRE RHEUMATISM CAM- PAIGN.	246-248

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ANNALS OF THE RHEUMATIC DISEASES

THE RHEUMATIC NODULES IN THE HEART

By LUDWIG ASCHOFF

IN 1904 Tawara and I, working in collaboration, decided that the formation of nodules in the heart was a characteristic change in rheumatic myocarditis. This latter term we used to describe a change which was the most significant local manifestation of rheumatic fever, or of specific infective rheumatism if one prefers the term recently used by Gräff. All authorities are today required to give more exact definitions of what they mean by "rheumatism." It must be admitted that this term has been used very loosely, and that it can never mean more than a symptom or group of symptoms which may appear in a variety of conditions. In this present paper I shall confine myself to that specific infective rheumatism, to use Gräff's term, or if one prefers it, the Bouillaud-Gräff disease.

The rheumatic nodules are found characteristically in this condition, and they are located for the most part in the heart muscle or in the pericardium. They may nevertheless be discovered, likewise, in the larger blood-vessels which arise from the heart, such as the aorta and the pulmonary artery, though here they are generally found in the parts which are also covered by pericardium. Nodules have also been discovered in the tendons of the musculature, in aponeuroses, the dura mater, the walls of the blood-vessels, and even in the skin in the neighbourhood of affected joints.

The terms "cardiac" or "visceral" rheumatism are used in order to describe those forms of rheumatism in which either the heart or the organs of the body are most affected. One has even heard the term "subcutaneous" rheumatism. Gräff has provided a very adequate description of the nodules found in the subcutaneous form of this disease, and has shown that they

bear a more or less close resemblance to nodules found in those conditions in which the viscera are most affected.

In this paper I will confine myself to a description of the rheumatic nodules which occur in the heart muscle, for these may be taken as the prototype of the granulomata which occur in rheumatism in general, and are in fact specific to these conditions. These rheumatic nodules, as seen in the heart muscle, are, if at all numerous, found to have a perivascular distribution. It is not common to find them spread further in the adjacent tissues. The nodules are formed from hypertrophied cells and are roughly cylindrical in shape. When the febrile stage of rheumatism has lasted for some time, the nodules gradually become scarred. In this way the non-specific but characteristic lesions round the vessels of the myocardium reach their final development.

In recent years two distinct objections have been advanced against our old conception of these appearances. It has been suggested that in the early stages of the disease the nodules become apparent as a result of a fibrinoid degeneration of the ground substance, this being particularly easily seen when Pap's stain is used. It is suggested that the cellular increase in the nodules is essentially secondary to the first change we have described. According to Klinge, the damage which develops in rheumatism occurs in all parts of the body, and in the first place involves the firm connective tissue. He thinks that the fibrinoid degeneration which follows, and which leads to the formation of the rheumatic nodules, is itself that stage in the process which is characteristic of the formation of these lesions.

The second objection is that the nodules are in no way specific to rheumatism. Nodules may occur in the heart muscle in scarlet fever which are indistinguishable from the others. In such cases I believe that there is a mixed infection with the scarlatinal toxin. Gräff has shown, as is admitted, that rheumatic infections appear to start from the same focus as does scarlet fever—namely, from the tonsillar tissue of the mouth and throat. For this reason the simultaneous appearance of rheumatic nodules and the infiltrations of scarlet fever in the heart muscle are not surprising. Attention was, at my instigation, also directed to this point by the investigations of I. W. Magladery and F. D. Billings (Stöber).

It is a striking fact that from time to time valvular lesions

of the heart are noted when scarlet fever has subsided. These may be explained by only one hypothesis, which is that in addition to the scarlet fever there has been a rheumatic infection in the sense already mentioned. In epidemics of pure scarlet fever valvular defects do not develop.

Masugi has recently drawn attention to the occurrence of rheumatic nodules in the heart muscle side by side with miliary tubercles. In my opinion we have in these cases also a mixed infection with the rheumatic virus and the tubercle bacillus. There is nothing surprising in the fact that when acute specific infective rheumatism develops, the tubercle bacillus is activated and brought into the blood stream. After all, the majority of human beings exhibit a primary focus in the lymph nodes round the hilus of the lung, and acute rheumatism, or the Bouillaud-Gräff disease, has a particular incidence on the heart and pericardium, which are close to the hilar regions of the lungs.

It is also very interesting to note that in miliary tubercle, as in streptococcal diseases, which may occasionally follow scarlet fever or acute rheumatism, one finds enlargement of the spleen. In uncomplicated acute rheumatism there is, according to Naegeli, no splenic enlargement at all.

I have said enough to refute the second theory which was advanced. Having surveyed the world literature I am still convinced that rheumatic nodules, as seen in the heart muscle, are specific to this rheumatic disease.

We must not neglect a consideration of the theories which try to account for the cellular hypertrophy in the nodules. I am giving now some pictures of a case of acute recurrent rheumatism involving the heart, which led to the death of a child aged six years. Despite the cellular overgrowth which has caused the formation of the nodules, there is no trace of a fibrinoid degeneration of the ground substance (Figs. 1, 2, 3 and 4). I therefore think that I have brought sufficient evidence to refute the ideas expressed in the systematic drawings made by Klinge. In this case in particular the multiplication of the cells was very marked.

Klinge has emphasised that even in the presence of cellular overgrowth fibrinoid degeneration is still easily seen. It is only when scar formation has occurred and the cells have shrunk down to form the nodule that the fibres return to the normal state.

"In this primary lesion, which exhibits a swelling of the

ground substance of the connective tissue with consequent degeneration, we believe that one sees the essential and specific change which is found in all rheumatic lesions known. From this primary lesion there develops—by multiplication of the mesenchyme cells—the cellular nodules" (F. Klinge, *Der Rheumatismus Ergeb. allgem. Path.*, 1933, xxvii. 32).

In the case we ourselves have described, typical rheumatic nodules are visible only here and there. In most of these one may see multinucleated or even giant cells. The latter may even be so numerous that the nodules, as may be seen in Fig. 6, resemble tubercles to some extent.

Anyone conversant with the case will nevertheless have no doubt that it was one of true acute rheumatism, and not miliary tuberculosis. In this case I also refuse to believe that there was any mixed infection. From the position of the nodules in the perivascular tissues, from their structure and the composition of their cells, I think tubercle may definitely be excluded.

The origin of the cells in the nodules has been a matter of dispute, but most of them are thought to be fibrocytes or histiocytes. No agreement on this matter has yet been reached. The sections which I am now showing do not help to a definite conclusion, although they are stained with pyronin. The question must therefore be allowed to remain open.

Both these types of cells occur in the connective tissue of the heart, and the following sentence, as printed in our first article on this subject, still holds good: "We think that there is no conclusive evidence which would make clear whether the cells are derived from the lymphocytoid elements or from the connective tissue" (p. 41). This statement is equally true if it is applied to the tubercle.

There is one further matter which needs discussion—namely, the part played by the granulocytes, especially the eosinophils, which ought to occur in large numbers if the nodule was the expression of an allergic phenomenon. I have stated in another place that the number of leucocytes in the nodules varied very greatly. As a rule one does not find granulocytes in the nodule itself, certainly not eosinophils. Such were our findings in the case now presented. Leucocytes in any number are only seen inside the nodule and in the area around it (Fig. 5). I think one may therefore say that the number of leucocytes in the nodule varies considerably.



FIG. 1.

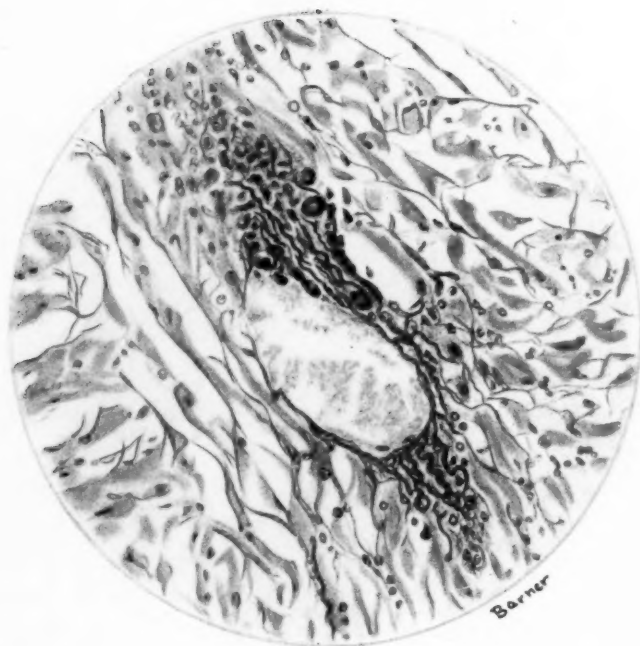


FIG. 2.

FIG. 1.—PERIVASCULAR NODULES FORMED OF NUMEROUS CELLS, SOME OF WHICH ARE MULTINUCLEATED.

Lymphocytes are seen in the surrounding tissues. Hæmatoxylin-eosin. ($\times 85$ times.)

FIG. 2.—CONNECTIVE TISSUE FIBRES ARE SEEN PASSING THROUGH A NODULE, BUT WITH NO DEGENERATIVE SOFTENING.

Multinucleated and giant cells are visible in that part of the nodule lying above the blood-vessel. Van Gieson's stain. ($\times 180$.)

Ludwig Aschoff.

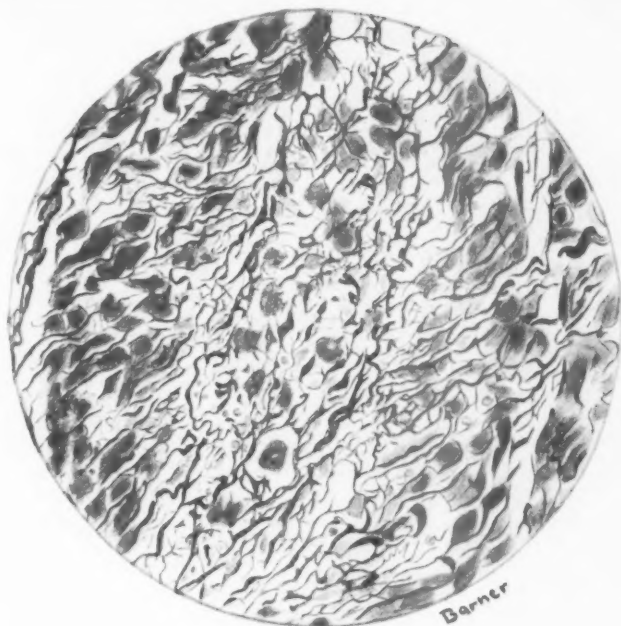


FIG. 3.



FIG. 4.

FIG. 3.—HIGHLY CELLULAR SPINDLE-SHAPED NODULE WITH MULTI-NUCLEATED AND GIANT CELLS.

The fibres are thrust apart, but not damaged (or warped).
Tibor-Pap stain. ($\times 180$.)

FIG. 4.—UNALTERED FIBRES TRAVERSE A RICHLY CELLULAR NODULE.
Very numerous lymphocytes. Tibor-Pap stain. ($\times 160$.)

Ludwig Aschoff.

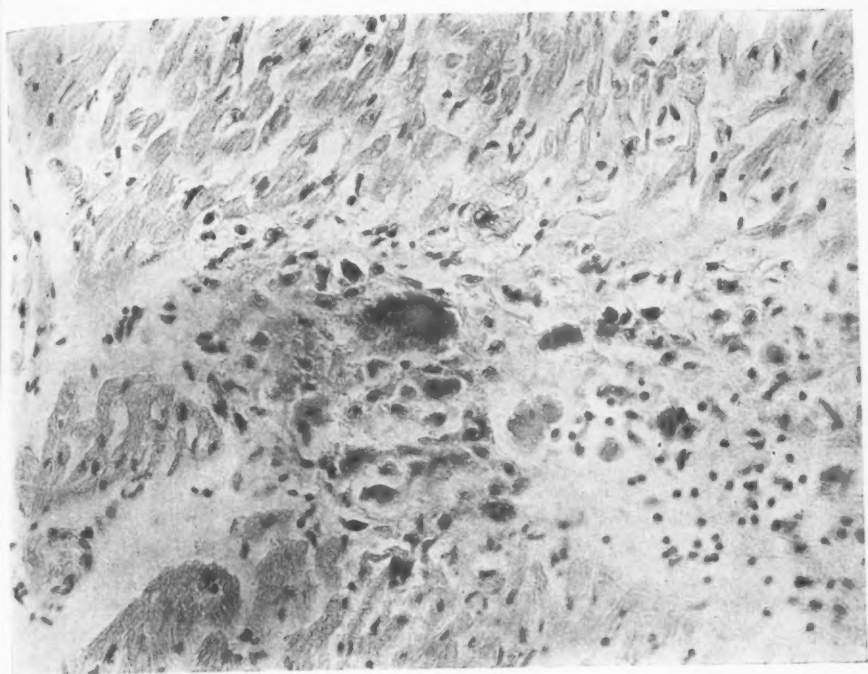


FIG. 6.—NODULE WITH MULTINUCLEATED GIANT CELL.
Note resemblance to a tubercle. Hematoxylin-
eosin. ($\times 200$.)

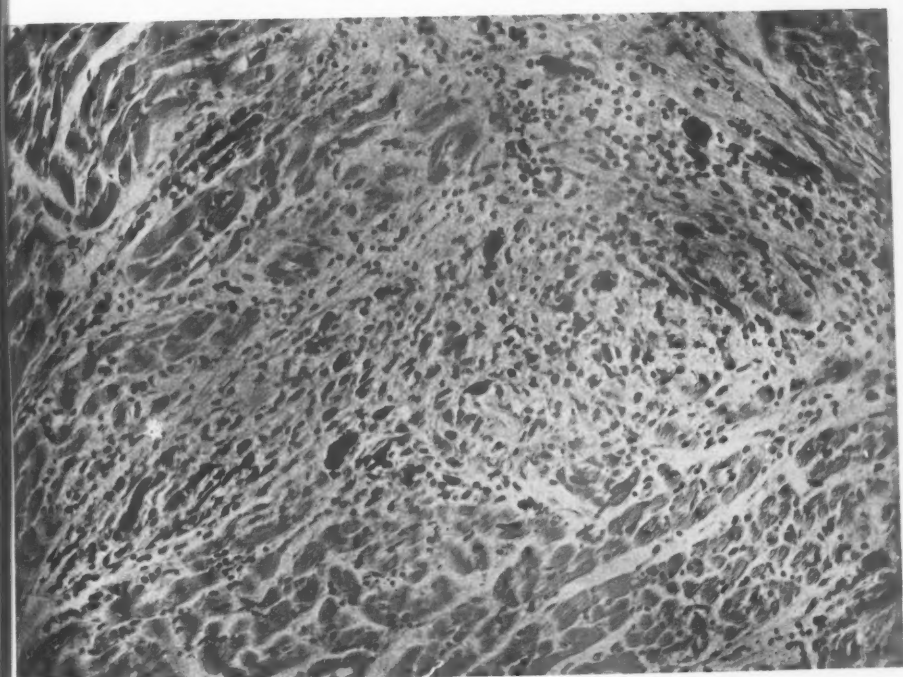


FIG. 5.—MULTIPLE NODULES WITH GIANT CELLS AND
LYMPHOCYTES IN THE SURROUNDING TISSUES.
Hematoxylin-eosin. ($\times 140$.)

It is possible that the proportion seen varies with the stage of development of the nodule, although in this acute and recent lesion no eosinophils can be seen. But the lymphocytes, in addition to the actual cells forming the nodule, play an important part.

The nodules are, as I have already stated, particularly rich in the characteristic cells. The cells may unite to form giant cells with two or more nuclei (Fig. 6). These do not, however, bear any marked resemblance to tuberculous giant cells. For the most part they are multinucleated structures such as may also be seen in osteoclasts. We may here again draw attention to the fact that some believe osteoclasts derive from the histiocyte cells, while others are inclined to group them with the fibrocytes.

As a result of my experiences I can state emphatically that the rheumatic nodules which appear in the myocardium are specific to the Bouillaud-Gräff disease (rheumatic fever). It is in no way essential that the formation of the richly cellular nodules should be preceded by fibrinoid degeneration of the ground substance. If the changes associated with scarlet fever or tuberculosis are seen side by side with what are certainly rheumatic nodules, then I consider the picture must necessarily be one of a mixed infection.

With these words I will conclude my remarks on the rheumatic nodules, which are cell formations specific to, and exclusively seen in, the Bouillaud-Gräff disease.

This paper has been translated from the German by Dr. G. C. Pether, to whom the author wishes to express his thanks.

A REVIEW OF RECENT ITALIAN WORK ON RHEUMATISM

I.—RHEUMATIC FEVER

By PAOLO RAVENNA

RHEUMATIC fever (Rh.F.) has recently been the object of numerous and extensive Italian studies. These have been carried out more especially in the University Medical Clinics directed by Professors F. Micheli (Turin), Ceconi (Turin) and Frugoni (Rome), and in the Institutes of Pathology directed by Professors Pepere (Milan) and Veratti (Pavia). The point of view of the Roman school was summarised by Chini and Lusena at the Congress of the International League against Rheumatism held in Moscow in May, 1934,²³ while that of the school of Micheli was explained by Andrei and myself⁹ in a lengthy report read before the Sixth National Congress for Microbiology held in Milan in April, 1937.

The most extensive researches have been directed towards the problem of ætiology. Some contributions to our knowledge of the clinical course, the differential diagnosis, and the pathology of the disease have also to be mentioned.

CLINICAL COURSE AND PATHOLOGY

The modern conception of Rh.F. considers it as an essentially chronic and cardiac disease presenting acute articular episodes during its course (Ehrström, Swift, etc.; Micheli,³⁴ Andrei and Ravenna^{9,10}). It is considered to be slightly infectious, arising not rarely in overcrowded houses (barracks, hospitals, colleges). The conception of the chronicity of Rh.F. is still disputed, and Ceconi in his treatise¹⁶ defines it as an acute disease, without, however, excluding the possibility of the contrary theory.

Rh.F. has recently been listed among the notifiable diseases in Italy, where statistical data on its frequency will be soon available. It may already be stated to be a very frequent disease in Northern Italy, especially in the regions with a continental climate.

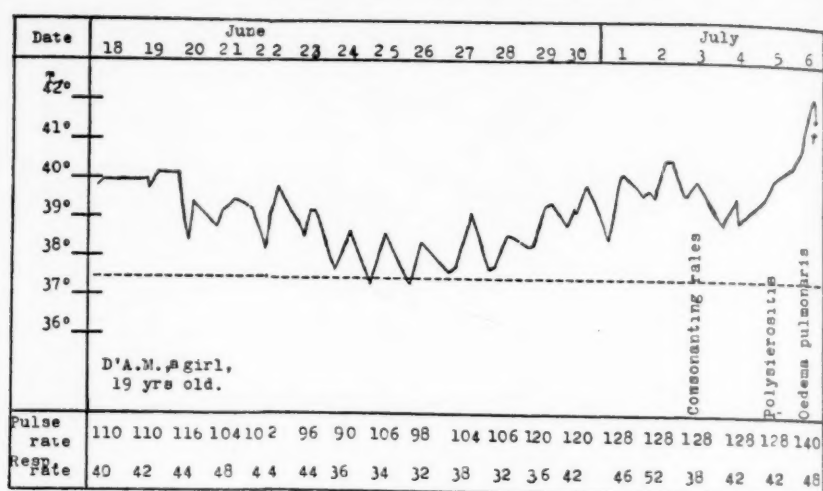


FIG. 1.—RHEUMATIC PNEUMONIA COMPLICATING ACUTE CARDITIS WITH POLYARTHRITIS AND POLYSEROSITIS IN A NINETEEN-YEAR-OLD GIRL DURING THE FIRST ATTACK OF RHEUMATIC FEVER.

Dyspnoea was already evident when signs of cardiac failure were still missing and two weeks before the appearance of pulmonary râles. Final stage occurred with hyperpyrexia and oedema pulmonaris, and death took place four weeks after the onset of rheumatic symptoms.

(From P. Ravenna, *Minerva Med.*, 1937.)

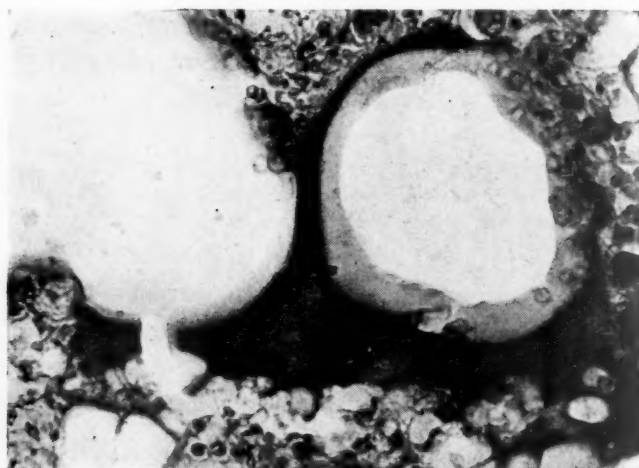


FIG. 2.—RHEUMATIC PNEUMONIA.

A view of pulmonary changes showing fibrinoid swelling in the walls of alveoles and respiratory bronchioles. Weigert's stain for fibrin. Enlarged about $\times 300$.

(From P. Ravenna, *Minerva Med.*, 1937.)

To the differential diagnosis of Rh.F. an important contribution has been brought by Micheli in his lectures on endocarditis lenta (subacute bacterial endocarditis). Further elements of differential diagnosis and a discussion on the relation of Rh.F. to some other diseases (sore throat, scarlet fever, serum disease, etc.) have been collected by Andrei and myself.⁹ The relation between Rh.F. and rheumatoid arthritis is still under discussion; most Italian authors believe that, while ætiological knowledge is still wanting, it is better to consider them as two different and autonomous diseases, though the present discrimination is based on quantitative rather than qualitative differences between the two clinical and pathological pictures, and cannot be looked upon as definite (Micheli,³³ Ceconi,^{16,17} Andrei and Ravenna,⁹ Robecchi⁴⁰).

Of the contributions to the pathology of Rh.F. I must quote the descriptions of rheumatic lesions in big veins and arteries (Cellina and De Angeli,¹⁸ Agostini¹) and in lymphatic glands (Cassano ^{14,15}), a study on Aschoff's nodules (N. Andreis), and the description of rheumatic pneumonia. The pathology of this rheumatic pneumonia is interesting also because it is different from that of any other known lung disease (Ravenna³⁹) (Figs. 1 and 2). A rheumatic nephritis has been described by Michelazzi and Turettini, but has been denied by Marcolongo.³²

For a diagnosis based exclusively on anatomical grounds the finding of typical Aschoff's bodies is of the greatest value. In a detailed paper published in 1934 I³⁶ have shown that, in contradiction to what had been asserted by some German authors, the finding of only degenerative (fibrinoid) or monocytic-histiocytic changes is not sufficient to authorise the anatomical diagnosis of Rh.F.

ÆTIOLOGY AND PATHOGENESIS

The conception of Rh.F. as an infectious disease has never been modified in Italy, not even by the voluminous literature, especially by German and Russian authors, in favour of an exclusively allergic and non-infective pathogenesis. This theory has never been taken into serious consideration, because Italian research work is based essentially on daily clinical observation. Any theory found to be in contrast with this is looked upon with suspicion. Roessle and Klinge's allergic theory, a revival of some old observations of Weintraud and Friedberger, has been

discussed and refuted by Micheli in a series of reports.³³ At the same time I showed on histological grounds that it is true that lesions similar to those of Rh.F. may be obtained with a more or less allergic treatment of experimental animals, but that these lesions are also obtainable with stimuli quite different from those which may be suspected in Rh.F.³⁶ The same point has been stressed by P. Locatelli and Varcica,⁴³⁻⁴⁷ on the basis of their experiments.

The allergic, non-infective, theory thus having been rejected, the infectious ætiology of Rh.F. has continued to be the leading line of Italian inquiries, and all research work has always been confined to the identification of an infectious causative agent.

TUBERCULOUS ÆTIOLOGY.—Discarding bacteria which have enjoyed but an ephemeral notoriety, the astonishing discovery of Reitter and Löwenstein has to be mentioned. In Italy, as everywhere, blood cultures carried out with Löwenstein's method gave only negative results (Favero, Alessi, Zuccola, Sigon, Schiavo, Arrigoni and Tronchetti,¹² Silvestrini⁴¹). Nor is the deviation of the complement by tuberculous antigen in Rh.F. patients (frequent according to Frola and Berio, rare according to Campus) of definite value in supporting this hypothesis.

STREPTOCOCCAL ÆTIOLOGY.—Among the other known bacteria, we have to consider only the streptococcus, or the different varieties of streptococci which, replacing one another in turn, have dominated the bacteriology of Rh.F. since the times of Löffler and Sahli, and since the first researches of F. J. Poynton and Paine in England, and of Allaria in Italy.

Most attempts to demonstrate the presence of streptococci in the blood or in the joints of rheumatic patients have given completely negative results to Gamna, Andrei, Ravenna, De Vecchi, Ceresoli, Virando, Malacrea and Belleli. Others (Corelli^{26, 27} and Chini²²) observed a slight bacteræmia set up by an hæmolytic or viridans streptococci; but the ætiological value of such a finding is lowered by the possibility of an identical bacteræmia following non-rheumatic sore throat, which was proved by the same authors in coincident inquiries.

The finding of streptococci in post-mortem examinations has also very little value, because of the frequency of agonal bacterial invasions, in which streptococci are often well represented (Andrei).

Streptococci have been found constantly only in rheumatic

throats, where one well-defined variety of hæmolytic streptococci has been isolated with high frequency during the sore throat accompanying or preceding the onset of Rh.F. This has been established by several American and English authors, and was confirmed also by some investigations of Andrei and myself.²

Some particular pathogenic activity, especially towards the joints and heart of experimental animals, has been sought in the streptococci obtained from Rh.F. patients. A selective tropism towards the joints was the first object of inquiry. A group of experiments conducted by the school of Frugoni (Lusena,²³ Chini,²¹ Magrassi, Garbini,²⁹ Spina⁴²) has been interpreted as positive—*i.e.*, demonstrating the possibility of an arthrotropism of streptococci. But with further experiments Andrei and I² have shown that rabbits, the animals used for this kind of experiment, present such frequent arthritis following the injections of any type of pathogenic streptococci, and that their individual susceptibility to this varies so much, that it is impossible to prove an arthrotropism with Rosenow's method. A lively polemic followed,³ with the result that no Italian author has any longer sustained the possibility of an arthrotropism, and only confirmations of our conclusions have appeared (Vacirca^{43, 46}).

It should be noted that the most difficult point in these inquiries on tropism lies in the evaluation of the results, which should be assessed by statistical methods. Indeed, only a quantitative and not a qualitative result is of value in these experiments, because we may obtain endocarditis or arthritis with any streptococcus; the crux is whether or not some streptococci give these lesions more frequently than others. I have attempted to ascertain whether the calculus of errors may be applied to the evaluation of such results. I have proposed³⁷ some new formulæ which are simple enough and may be useful for this purpose. They show the limits between which the errors of a certain group of experiments are probably comprised, and they enable us to compare different series of experiments, defining their relative values. The employment of these formulæ for the evaluation of experimental results on tropism leads precisely to the above-mentioned conclusions.

More involved technical procedures have been employed in further inquiries: a streptococcal focus of infection has been produced in rabbits, and some days after a suspension of the same bacteria killed has been given intravenously. This technique

ought roughly to reproduce what may happen in human patients if a circumscribed streptococcal infection changes the body reactivity in such a manner that the successive entry into the circulation of toxins from the same focus may produce the articular and cardiac symptomatology of Rh.F. Such kinds of experiments tried by some American and Russian authors have given negative results. But Magrassi has claimed some very interesting positive results, having obtained with nearly absolute regularity a true granulomatous spread throughout many joints and in the heart, where he stressed the finding of Aschoff-similar nodules containing monocytes and histiocytes, as well as some giant cells.

Andrei and I⁴ repeated these attempts, with some modification in the technique, to elucidate their significance. The changes obtained by us have always been confined to the heart and to the one joint in which an injection of living streptococci had been given; widespread changes throughout many joints have been always missing. Morphologically the lesions observed by us in rabbits' hearts have been at times very similar to those of rheumatic myocarditis, but no macroscopic or microscopic endocarditis has been found. The joint lesions showed the classical features of a chronic or of a healing pyogenous infection. Further researches that we made have explained the meaning of the myocardial changes; these lesions are to be observed in rabbits following extremely diverse treatments, and also without treatment, for it is well known that rabbits are often subject to spontaneous chronic myocarditis. These changes have, however, no right to be considered as specific for any one ætiology or any one pathogenesis, and cannot serve to demonstrate the ætiopathogenesis of human Rh.F. The experiments of Andrei and myself on focal infection have been repeated and confirmed by Vacirca,^{44, 45, 47} who worked for some time in Aschoff's Pathological Institute in Freiburg. Later Chini and Magrassi³¹ have associated themselves with our conclusion. They have interpreted the granulomatosis obtained with focal infection in rabbits as a consequence of a mild septicæmia originating from the focus; these changes may well reproduce the picture and the pathogenesis of streptococcal rheumatism (Gräff), but have no bearing on true Rh.F.

Some positive cutaneous reactions towards streptococci and the possibility of agglutinating the streptococci with the serum of rheumatic patients have been claimed by Chini and Magrassi.²⁴ But for the ætiological investigation of Rh.F. they are of little

importance, because of the small number of patients studied, and because of the positive occurrence of similar reactions in non-rheumatic patients.

VIRUS ÆTIOLOGY.—Direct search for a virus in the blood or other organic fluids of rheumatic patients has been attempted by Sindoni and Vitetti. In 1924 they claimed to have found a filtrable virus which in cultures was said to have the form of a diplococcus. Control inquiries by Gamna and Andrei gave negative results, and in a short time silence descended over these researches.

Another group of inquiries have been made by de Vecchi, Gennari, Natali, Vanni, Magrassi. They have injected rheumatic patients' blood into laboratory animals; the results have been either positive, but not confirmed, or negative. These attempts have been given up.

In 1932, after a thorough and critical review of the results obtained by the former authors, I proposed³⁶ to take up these experiments again by injecting blood (or eventually other pathological material) taken from patients with Rh.F. I set down the following experimental rules: (1) Blood to be injected as soon as taken from the patient, and without being modified by anticoagulants. Whole blood and not serum to be used, as the latter is generally poorer in germs. (2) Injections to be given in a cavity whence the blood may be quickly absorbed (*e.g.*, abdominal cavity), and not in the veins, where it might produce vascular or cardiac thrombosis. (3) Rabbits appear to be the most suitable animals for large-scale researches, their viscera being big enough for an easy macroscopic examination. (4) Only young rabbits to be used, as they are usually more sensitive to infection than older ones. (5) After the injection the animals to be observed for rather a long time (at least three to four weeks), because the development of characteristic changes in Rh.F. always requires some weeks.

These researches were undertaken with the collaboration of Dr. G. Andrei, a bacteriologist, and have been carried on over five years. The results, which were published in several papers,^{5, 6, 7, 8, 11} are based on 947 rabbits, one to two months old, which we received from diverse breeding-places of the province of Turin.

Three to four weeks after one injection of 5 to 10 c.c. per kg. of whole blood taken from rheumatic patients and given in the



Fig. 3.



Fig. 4.

FIGS. 3 AND 4.—ENDOCARDITIC LESIONS IN THE RIGHT VENTRICLE RESULTING FROM THE INJECTION OF RHEUMATIC BLOOD.

Fig. 3: Heart of the rabbit, No. 354. (Slightly enlarged photograph.)

Fig. 4: Heart of the rabbit, No. 831. (Drawing from Andrei and Ravenna, *Arch. of Intern. Med.*, 1938.)



FIG. 5.—SECTION OF A LARGE THROMBUS OF THE TRICUSPID VALVE OF A RABBIT KILLED FORTY-FOUR DAYS AFTER THE INJECTION OF BLOOD FROM ENDOCARDITIC RABBIT.

Hæmatoxylin stain.

(From Andrei and Ravenna, *Arch. of Intern. Med.*, 1938.)

peritoneal cavity, on killing the animals a widespread endocarditis was found to be present in about 40 per cent. of the injected rabbits (Figs. 3, 4 and 5). This endocarditis is very similar to the rheumatic one, both because of its morphology and because of the constant sterility of the pathological tissues, which have been tested by routine bacteriological examination. The endocarditis may be transmitted to other rabbits by means of whole blood or filtered blood from endocarditic animals; positive serial transmission has been obtained through five successive passages. Transmission has been obtained also with a suspension containing only a small quantity of thrombotic material. The possibility of obtaining an endocarditis in non-injected rabbits kept in cages together with endocarditic ones has also been shown. No similar change, either spontaneous or experimentally induced, has been observed by the forementioned workers. Several hundreds of control rabbits have been examined concurrently with the principal experiments; they have shown that a spontaneous thrombo-endocarditis may have occurred in our animals, but so rarely that it could not modify the significance of the experiments (0.5 to 1 per cent.). The examination of our rabbits has always been extended to the whole body. But no change has been found, with the exception of the usual myocarditis that is frequent also in non-treated rabbits. In another series of experiments the pathogenic power of blood taken from non-rheumatic patients has been tried. It has resulted that also this blood may produce endocarditis, but with a lower frequency than the rheumatic one (18 per cent.). Finally, sterile milk and sterile horse serum have given positive results, and, after the usual incubation time, endocarditis appeared once again, with a high frequency (30 per cent.).

On this experimental evidence Andrei and I have concluded that endocarditis in rabbits is a disease which, though occasionally spontaneous, may be obtained with various treatments, consisting essentially in injection of heterogeneous protein. Its true nature should be infectious and probably contagious. The apparent sterility of viscera and blood of affected animals has enabled us to ascribe the disease to an unknown virus, probably an *infra-virus*.

Our experiments have been controlled by Chini,¹⁹ who, in researches conducted according to our technique, has obtained the same changes. Chini has pointed out the nearly absolute

identity of these experimental lesions with those of human rheumatic endocarditis.

The importance of these results is very difficult to estimate: opinions can but wander in the realm of hypotheses. The possibility that rabbit's endocarditis may be due to the agent of human endocarditis is hardly likely. In fact, it is possible to produce the disease in rabbits with non-rheumatic blood and with protein of proved sterility. But why, then, does rheumatic blood induce endocarditis more frequently than non-rheumatic blood? Does a substance having a special tendency to produce endocarditis exist in rheumatic blood? These are questions which further experiments may answer.

If we admit that the supposed endocarditic virus is a frequent or a constant guest of rabbits, and that it is activated by non-specific injections of protein, may this finding have any importance for the pathogenesis of rheumatic endocarditis? A definite answer is as yet impossible; but it should be pointed out that these researches may lead to very interesting results. They should enter into a field as yet nearly unexplored, that of biotropism (activation of a latent virus by material of bacterial or non-bacterial origin). The study of biotropism, just begun in experimental animals, will probably reveal un hoped-for applications to human pathological conditions. A frequent example of biotropism in man is that which occurs in herpes febrilis; its agent, a virus which may be a harmless guest of the human body, induces herpes during some other disease, generally due to cocci (pneumococci, meningococci, etc.). Nothing excludes the supposition that a similar phenomenon may occur in Rh.F.—i.e., that a virus, which should be present and latent in the body, may become pathogenic for its guest on account of a streptococcal infection, like the sore throat which so frequently precedes the onset of rheumatic activity.

The hypothesis that the causative agent of Rh.F. is a virus, but that a symbiotic association with streptococci is more or less necessary for the onset of the disease or of its relapses, is not based solely on the results of the above-mentioned experiments. Such a conception I have already put forward three years ago, on the basis of clinical, epidemiological and bacteriological evidence.³⁵ It is impossible to resume here all the arguments, but I would stress its chief basis, which consisted of the results of very important work by English and American authors.

Rh.F. begins very often following a streptococcal throat infection, but it continues a long time after the disappearance of the streptococci from the throat, showing a quite independent further development. Lately Coburn and Moore have brought forward another important argument: sulphanilamide administered to rheumatic subjects after the onset of streptococcal throat infections does not prevent rheumatism, but when taken prophylactically by rheumatic subjects who escape streptococcal infection, they do not show signs of rheumatic activity. In conclusion, these researches may show that the importance of streptococci is confined to the onset of Rh.F., because its continuation is autonomous and due to a different causative agent, the activity of which seems not to be influenced by sulphanilamide.

"The possibility of a virus ætiology has undoubtedly received more attention in Italy than in any other country" (F. J. Poynton and B. Schlesinger, "Recent Advances in the Study of Rheumatism," London, 1937), but latterly it has acquired a growing interest also in other countries. In England, Schlesinger, Signy and Amies in pathological fluids taken from rheumatic patients and submitted to high-speed centrifugation have found particles similar to those of other known virus diseases. These particles have been agglutinated by rheumatic patients' serum, but all attempts to show their pathogenic power have, up to date, been unsuccessful. In the Rockefeller Institute for Medical Research in New York, H. F. Swift, after devoting more than fifteen years to the study of the importance of streptococci in Rh.F., has attempted to inoculate the chorion-allantoic membrane of chicken embryos with rheumatic exudates. He claims to have isolated a filtrable virus. These results are as yet too recent to permit a definite conclusion.

In conclusion, it appears that the research work is actually finding its way towards the discovery of a new virus as the agent of Rh.F. The researches, which should be continued along three main avenues of inquiry, bacteriological, clinical and epidemiological, are neither easy nor rapid, but the better knowledge of a disease such as rheumatic fever, with its immense social and economic importance, is worth any effort.

(To be continued.)

For References see pp. 178-179.

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THE FORMOL-GEL REACTION AND ERYTHROCYTE SEDIMENTATION RATE IN ACUTE RHEUMATISM

BY C. A. GREEN, S. THOMSON, AND A. J. GLAZEBROOK

INTRODUCTION

GATÉ and Pappacostas (1920) observed that the addition of formaldehyde to Wassermann-positive sera resulted in the solidification of 85 per cent. of specimens, while approximately the same proportion of Wassermann-negative sera failed to react in this way. They suggested that this reaction was due to an abnormal distribution of serum proteins. Holborrow (1922) found that forty-five of sixty-four Wassermann-positive sera gave a positive formol-gel reaction, and also seventeen of eighty-nine Wassermann-negative sera. He concluded that the gelation was due to direct action of the formalin on the serum proteins, and from experimental work considered it probable that acid-protein produced a gel with formalin, while alkali-protein had not this property. Napier (1921-22) and Spackman (1921) observed a similar phenomenon in kala-azar, but noted a difference in appearance between the gelation in that disease and in syphilis. In kala-azar the serum became opaque and very firm in consistence, as though inspissated, within a few minutes, whereas gelation was relatively delayed in syphilitic sera, taking up to twenty-four hours to appear, and the gel formed was soft and transparent.

As regards the correlation of the formol-gel test with other biological tests, Napier and Henderson (1931) first observed parallelism with the erythrocyte sedimentation test in kala-azar, but they considered the formol-gel test was inferior for diagnostic or prognostic purposes. Pfeffer (1925) stated that the formol-gel test was positive in a proportion of cases of chronic rheumatism and of tuberculosis of the exudative type. Gibson (1938) applied the test, in parallel with the erythrocyte sedimentation rate, to a series of 100 cases of chronic rheumatism. Using plasma, he found that the formol-gel test was negative in 40 of 42

cases with normal sedimentation rates, and positive in 33 of 34 cases with markedly increased sedimentation rates. Approximately half the cases showing a moderate increase in sedimentation rate were positive. He noted a very close parallelism between the two tests, and considered that it may be of use as an additional pathological criterion of activity in chronic rheumatism. Gibson emphasised that the formol-gel test was less sensitive than the sedimentation test in finding evidence of activity in early cases, and considered that it should be used as a supplementary, but not substitute test. On the other hand, Schultz and Rose (1939) expressed the opinion that, whereas in various febrile illnesses other than rheumatic fever a close parallelism was demonstrable between the erythrocyte sedimentation rate and the formol-gel reaction, unique results were obtained in rheumatic fever. Early in the course of illness negative formol-gel reactions were frequently associated with very rapid sedimentation rates, while after the development of active carditis positive gel reactions often appeared when the sedimentation rate was reverting to normal limits. They concluded that the formol-gel reaction was of value in determining the presence of active carditis in patients known to be suffering from rheumatic fever.

This paper records observations on both tests in a group of young male adults in the various phases of acute and subacute rheumatism.

METHODS

DETERMINATION OF ERYTHROCYTE SEDIMENTATION RATE.—10 c.c. of venous blood was thoroughly shaken with 0.02 gm. neutral potassium oxalate in a screw-cap bottle. The Zeckwer and Goodell (1935) method was adopted in principle. Within three hours of the collection of the specimen a 5 c.c. centrifuge tube, graduated in 0.05 c.c., was filled to the 5 c.c. mark with oxalated blood. The volume of the sedimented red cells was noted after one hour at room temperature. This result was expressed as the percentage volume of red cells, the percentage sign being omitted—*e.g.*, E.S.R. 60 indicates that the volume of red cells, after one hour, was 60 per cent. of the total volume of blood. It should be noted that any increase in this figure is interpreted as an approximation to the normal. This reading is, therefore, the reverse of the more usual method of expressing

the sedimentation rate as the length of the cleared plasma column above the sedimented cells.

HÆMATOCRIT VOLUME.—The graduated tube containing 5 c.c. blood was centrifuged for fifteen minutes at 3,000 revolutions per minute, and the packed red-cell volume expressed as a percentage of the whole blood volume.

FORMOL-GEL TEST.—The supernatant plasma in the centrifuge tube was then separated for the formol-gel test, the quantitative method suggested by Gibson (1938) being used. The only modification introduced was the reduction to half-volume of the various reagents, the relative proportions remaining the same, as follows:

	Tube :	1	2	3	4	5	6	7
Plasma	..	0.5	0.45	0.4	0.35	0.3	0.25	0.5
Saline	..	0.0	0.05	0.1	0.15	0.2	0.25	0.0
18% formalin		0.04	0.04	0.04	0.04	0.04	0.04	0.0

The tubes were placed in a Wassermann rack supported at one end so that the long axis of the tubes was nearer the horizontal than the vertical plane. After eighteen hours at room temperature the sloped tubes were returned to the vertical position and the occurrence of solidification noted. The results were expressed as follows:

- 1+ } Degrees of partial coagulation of undiluted plasma.
 2+ }
 3+ : Complete coagulation of undiluted plasma.
 4+ : Complete coagulation of plasma diluted 0.9 in 1.
 5+ : Complete coagulation of plasma diluted 0.8 in 1.
 6+ : Complete coagulation of plasma diluted 0.7 in 1.
 7+ : Complete coagulation of plasma diluted 0.6 in 1.
 8+ : Complete coagulation of plasma diluted 0.5 in 1.

N.B.—The following contractions will be used in the text:

E.S.R.: Erythrocyte sedimentation rate.

H.V.: Hæmatocrit volume.

F.G.T.: Formol-gel test.

RESULTS

Before attempting to correlate the E.S.R., H.V. and F.G.T. results, certain basic data were required. The majority of the subjects studied were aged sixteen to eighteen years, and it was considered desirable to ascertain the average or normal limits of these tests in health for this particular age-group and community. All patients were serially tested at the end of prolonged convalescence when about to be discharged as fit. The distribution

of the E.S.R. results at this time is illustrated in Chart 1. Although the majority of the tests upon which this chart was constructed were obtained from rheumatic subjects, a few patients completely recovered from scarlatina and from tonsillitis were included. The series was therefore constituted as follows: 107 tests from 76 rheumatic patients, single tests from 7 cases of scarlatina and from 11 cases of post-tonsillitis patients. Chart 1 indicates that at the end of convalescence the E.S.R. was most frequently at the 95-96 level, the next largest groups being immediately adjacent to the latter. The average E.S.R.,

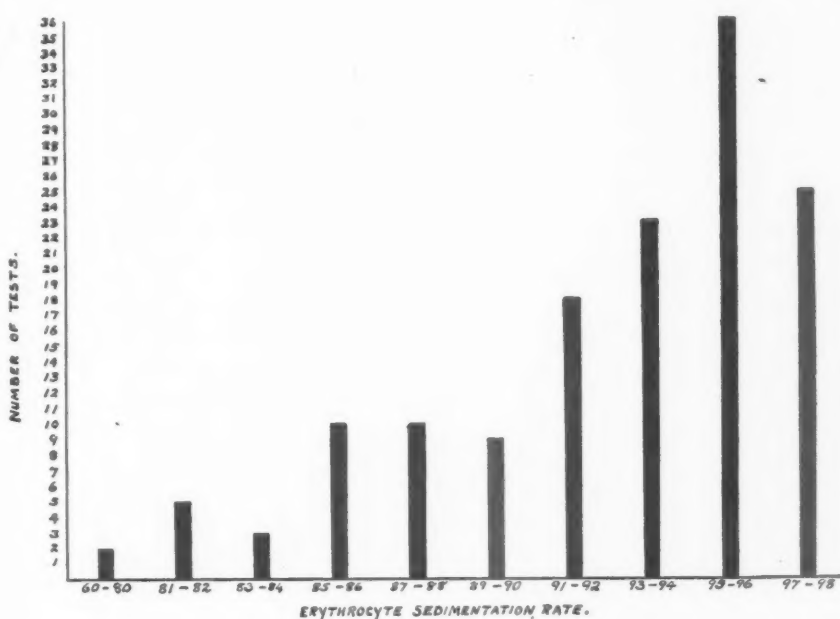


CHART 1.

determined by dividing the total of all E.S.R. results by the number of tests, was found to be 92.4. Table I. shows even more significantly the high E.S.R. of patients on discharge from hospital, 75.2 per cent. of specimens being over 90 and 99.2 per cent. over 80. For this reason it was concluded that, although an E.S.R. between 80 and 90 could be considered as possibly abnormal, an E.S.R. below 80 was almost certainly abnormal.

In the same way data on the H.V. of boys on discharge in health were sought. Chart 2 shows that the mean figure was most frequently at the 46-48 level, while the distribution of results

on either side of this group fell in the expected manner. The average H.V., determined as above, was 47.9. Table II. shows that the H.V. of 81.4 per cent. of specimens was 45 or higher, and in every case was above 40. All hæmatocrit volumes lower than 40 were therefore considered to be almost certainly abnormal, and those between 40 and 45 as possibly, but not commonly, in the same category.

ERYTHROCYTE SEDIMENTATION RATES AND FORMOL-GEL TEST IN RHEUMATISM.—Both tests were applied in parallel in a series of 102 cases of rheumatism in the acute, subacute and

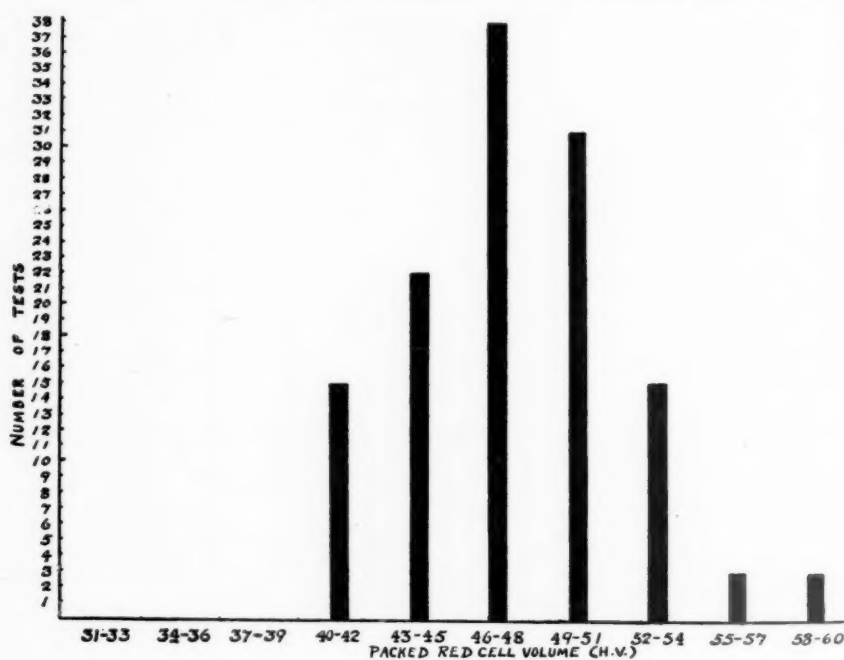


CHART 2.

convalescent phases. Of this group, 96 cases were boys, aged sixteen to nineteen years, who had been living for some months under similar environmental conditions. The combined results are grouped in Table III. Only 2.6 per cent. of 266 specimens with an E.S.R. over 80 gave a positive F.G.T., as compared with 97.1 per cent. of specimens with an E.S.R. lower than 60. Approximately half the cases with an E.S.R. between these limits were positive. In Table IV. the correlation is indicated in greater detail. Only one positive F.G.T. was found in a series of 173 tests when the E.S.R. was above 90, whereas every E.S.R.

below 50 was accompanied by a positive F.G.T. The intervening groups were proportionately related. A further point of interest in the table is that 70.8 per cent. of positive F.G. tests were recorded in 161 specimens with an E.S.R. below 80, as compared with 2.6 per cent. of 266 specimens in the group above 80. On grouping the positive F.G.T. results at various levels of the E.S.R., as in Table V., there was demonstrated a progressive increase in the mean F.G.T. result as the E.S.R. level fell.

HÆMATOCRIT VOLUME AND FORMOL-GEL TEST IN RHEUMATISM.—Following the method of comparison used by Gibson (1938), Table VI. shows the mean E.S.R. and mean H.V. of specimens grouped according to the results of the F.G.T. A reduction in intensity of the positive F.G. reaction was accompanied by progressive increase of the mean E.S.R. and mean H.V. The only exception to be noted in the table was the slightly higher mean H.V. of 40.3 in the 5+ F.G. group as compared with 39.2 in the 4+ F.G. group. Otherwise the correlation was complete. The negative F.G. group included specimens taken in early as well as in late stages of illness, and hence the mean S.R. and H.V. values of 86.6 and 44.1 respectively were lower than those determined at the end of convalescence in the preliminary group, in which the formol-gel test was invariably negative.

Table VII. shows the percentage of positive F.G. tests at various levels of the H.V. It will be seen that the F.G.T. was positive in 48, or 92.3 per cent., of 52 specimens with an H.V. lower than 40, as compared with 2, or 1.8 per cent., of 113 specimens with an H.V. above 50. Between these two levels, 26.6 per cent. of specimens reacted positively to the F.G.T.

FAILURE IN AGREEMENT OF TEST RESULTS

The instances in which the E.S.R. and F.G.T. failed to give comparable results may now be considered.

E.S.R. WITHIN NORMAL LIMITS, F.G.T. POSITIVE.—Taking 80 as the lower limit of normality for the E.S.R. test, 7 specimens were found to give a normal E.S.R., but positive F.G.T.

CASE 1				
	E.S.R.	H.V.	F.G.T.	Week of Illness.
	86	45	Negative	5th.
	88	48	Negative	7th.
First discrepancy	94	38	1+	9th.
	94	48	Negative	11th.

This was the only case in which an E.S.R. greater than 90 was accompanied by a positive F.G.T. As seen in the serial record, the F.G.T. was a weak positive.

CASE 2

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
	63	45	2+	8th.
Second discrepancy ..	82	50	1+	10th.
	92	44	Negative	12th.
	82	51	Negative	13th.

From the eighth to the tenth week of illness there was a marked improvement in the E.S.R., but the F.G.T. was still weakly positive during this transition period.

CASE 3

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
	70	40	3+	4th.
Third discrepancy ..	80	44	2+	6th.
Fourth discrepancy ..	82	44	1+	9th.
	82	40	Negative	14th.

Again, during a transition period in the patient's progress the E.S.R., while in the limits of normality, was accompanied by a positive F.G.T.

CASE 4

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
	79	45	3+	3rd.
Fifth discrepancy ..	82	50	3+	4th.
Sixth discrepancy ..	80	48	3+	6th.
	90	49	Negative	8th.

Disagreement occurred in the fourth and sixth weeks of a relapse when joint pains and pyrexia were still present. The result of the F.G.T. was a more reliable indication of the clinical condition than the E.S.R.

CASE 5

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
	91	50	Negative	1st.
Seventh discrepancy ..	86	36	3+	2nd.

In this early case stiffness and pain on movement of the leg were the only symptoms present.

In this group, therefore, there was no serious degree of disparity between the results of the two tests.

E.S.R. BELOW NORMAL LIMITS, F.G.T. NEGATIVE.—In 47 specimens with a negative F.G.T. the E.S.R. was below 80.

As seen in Table IV., 31 of these were in the group with an E.S.R. between 79 and 70, and could be considered as border-line cases similar to those above. The remaining 14 discrepancies of greater degree were as follows:

CASE 6

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
	94	50	Negative	12th.
	90	46	Negative	14th.
First discrepancy ..	58	42	Negative	18th.
	75	44	Negative	20th.

On returning from four weeks' sick-leave, eighteen weeks after the onset of illness, no clinical abnormality was detected to account for the abnormal E.S.R.

CASE 7

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Second discrepancy ..	50	42	Negative	1st.
	65	42	3 +	2nd.

In this early case there was a definite lag in the appearance of the positive formol-gel reaction.

CASE 8

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Third discrepancy ..	66	45	Negative	2nd.
	88	49	Negative	4th.
	80	47	Negative	5th.
	92	48	Negative	6th.
	94	50	Negative	8th.
	60	42	1 +	10th.
	46	37	5 +	12th.
	80	42	Negative	15th.

Examined for the first time in the second week of illness, the E.S.R. was definitely abnormal, while the F.G.T. was still negative. The ensuing seven results were in agreement.

CASE 9

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Fourth discrepancy ..	69	50	Negative	1st.
	72	70	5 +	3rd.
	56	79	8 +	4th.
	58	62	4 +	5th.
	60	64	5 +	6th.
	66	62	5 +	7th.
	52	62	5 +	9th.
	62	72	1 +	11th.

In this case, also, there was a definite lag in the appearance of the positive F.G.T., but thereafter the two tests approximated closely.

CASE 10

		<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
		62	42	5 +	2nd.
		68	42	6 +	3rd.
Fifth discrepancy	..	64	45	Negative	6th.
		60	44	4 +	7th.
		55	42	4 +	9th.
		64	45	2 +	11th.

After being strongly positive in the second and third weeks the F.G.T. was negative in the sixth week, while the E.S.R. remained at the same low level as in the previous weeks. In the subsequent tests the results were in agreement. No explanation for this discrepancy was discovered.

CASE 11

		<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
		96	50	Negative	2nd.
		85	44	Negative	3rd.
		72	45	3 +	4th.
Sixth discrepancy	..	65	42	Negative	5th.
Seventh discrepancy	..	62	41	Negative	7th.
		73	46	Negative	9th.
		90	45	Negative	11th.

In the fourth week of illness a fall in the S.R. was accompanied by complete gelation of the plasma. In the following four weeks a still further fall in the E.S.R. occurred, but the F.G.T. had returned to normal limits.

CASE 12

		<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
		76	48	3 +	2nd.
		74	43	3 +	4th.
		50	40	3 +	5th.
		65	40	4 +	6th.
Eighth discrepancy	..	60	40	Negative	7th.
Ninth discrepancy	..	62	40	Negative	9th.
		75	40	Negative	11th.
		77	40	Negative	13th.

In this case the F.G.T. had returned to the negative phase at least four weeks before improvement in the E.S.R. began.

CASE 13

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Tenth discrepancy ..	67	42	Negative	3rd.
	77	46	Negative	5th.
	85	50	Negative	6th.
	96	45	Negative	7th.
	96	50	Negative	9th.

This patient was examined for the first time in the third week of illness, when no acute symptoms were present. The *E.S.R.* was then abnormal, but the *F.G.T.* negative.

CASE 14

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Eleventh discrepancy ..	50	40	5 +	1st.
	46	37	6 +	2nd.
	57	35	6 +	3rd.
	46	38	4 +	4th.
	60	50	Negative	5th.
	45	36	4 +	6th.
	51	42	3 +	8th.
	82	42	Negative	10th.

This disagreement in the fifth week was due to the partial clotting of the blood specimen in the collection bottle. Complete agreement was found at all other times.

CASE 15

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Twelfth discrepancy ..	74	40	Negative	4th.
	70	40	Negative	6th.
	68	39	Negative	8th.
	60	40	Negative	10th.
Thirteenth discrepancy ..	60	40	Negative	10th.

Despite the fall in the *E.S.R.*, the *F.G.T.* remained negative in the eighth and tenth weeks.

CASE 16

	<i>E.S.R.</i>	<i>H.V.</i>	<i>F.G.T.</i>	<i>Week of Illness.</i>
Fourteenth discrepancy ..	95	44	Negative	2nd.
	60	45	Negative	3rd.
	79	40	2 +	4th.

In this last series of 14 discrepancies, the first 2 were the only specimens out of 75 with an *E.S.R.* below 60 which gave a negative *F.G.T.* The remaining examples were mainly borderline cases occurring at some transition period in the course of illness. These detailed examples otherwise serve to illustrate

the correlation which can be expected between these two tests during the course of the infection.

EFFECT OF DELAY IN SEDIMENTATION RATE AND FORMOL-GEL TEST.—It is well recognised that there must be the minimum delay in setting up blood for the E.S.R. after the sample has been taken. This may introduce practical difficulties in obtaining results under standardised conditions, particularly if the laboratory be at some distance from the clinical material. For interest, preliminary investigations were made on the relative effect of delay on the E.S.R. and F.G.T. results. In 105 consecutive specimens both tests were carried out within three hours of collection, as in the routine method described previously. The E.S.R. and F.G. tests were then repeated twelve and twenty-four hours respectively, after the collection of blood. As shown in Table VIII., the sedimentation rate was markedly affected by delay, there being an increase in the twelve-hour E.S.R. in 77.1 per cent. of specimens. In 22 instances an E.S.R. below 80 at three hours was above that level after twelve hours, the increase sometimes being very marked—*e.g.*, 62 to 89, 65 to 93. The formol-gel reaction was found to be much more stable, as Table IX. indicates. Although the period of delay was twice that introduced in the case of the E.S.R., there was no change in the twenty-four-hour F.G.T. result in 80.9 per cent. of specimens. Such variation as did occur was always slight, and never greater than 1+. Only one specimen, initially negative, developed a weak 1+ positive F.G.T. on repetition, and all positive results were confirmed by the second test.

DISCUSSION

It is of great importance that any method of determining the activity of rheumatic infection should be fully investigated, even though the results of the test be non-specific in nature. This investigation supports the conclusions of Gibson (1938) that the formol-gel test is of value in supplementing the erythrocyte sedimentation test. The correlation in results corresponded very closely to those noted by Gibson, and outstanding discrepancies were rarely encountered. This finding is not in accord with the observations of Schultz and Rose (1939). In Table X. the two series of results are contrasted. It will be seen that Schultz and Rose noted 36.1 per cent. of positive formol-gel

tests in specimens with markedly abnormal erythrocyte sedimentation rates—*i.e.*, 100+ (Schultz)—as compared with 97.6 per cent. in the present series. On the other hand, Schultz and Rose found that 18.5 per cent. of specimens with an erythrocyte sedimentation rate of 20 or less (Schultz) gave a positive formol-gel test, as compared with only 2.4 per cent. in the present series. A possible explanation for these divergent results was the greater frequency of delayed but persistent formol-gel reactions in the series recorded by Schultz and Rose. In the present investigation it was found that, in general, a change from a normal to an abnormal result in one test was synchronous with a similar change in the other. As compared with the sedimentation rate, there may be delay both in the appearance and disappearance of a positive gel reaction, as noted by Schultz and Rose (1939), but the positive gel reaction may precede the appearance of the initial abnormal result in the sedimentation rate.

In its quantitative form the formol-gel test furnished useful information regarding the progress of the individual case. Its utility becomes even greater if there is any possibility of delay in the examination of specimens. The preliminary work has shown that such delay, even up to thirty-six hours after the collection of blood, had little or no effect on the formol-gel test, whereas any delay beyond three hours or less may completely invalidate the results of the erythrocyte sedimentation rate.

CONCLUSIONS

1. The average erythrocyte sedimentation rate, as determined by the method of Zeckwer and Goodell (1935), and expressed as the percentage red-cell volume, in a group of male rheumatic convalescents aged sixteen to nineteen years was 94.4, and the average hæmatocrit volume 47.9. The formol-gel test was invariably negative.

2. In 99.2 per cent. of cases, on discharge from hospital the erythrocyte sedimentation rate was over 80, and in 81.4 per cent. of cases the hæmatocrit volume was 45 or over.

3. 464 results of erythrocyte sedimentation rate and formol-gel tests on blood specimens from 102 cases of acute rheumatism are compared. Positive formol-gel reactions occurred in 97.1 per cent. of specimens with an erythrocyte sedimentation rate

below 60, as compared with 2·6 per cent. in specimens with rates above 80.

4. In 92·3 per cent. of 54 specimens with hæmatocrit volumes less than 40 gave a positive formol-gel reaction.

5. The formol-gel reaction was much less affected by delay than was the erythrocyte sedimentation test.

TABLE I.—ERYTHROCYTE SEDIMENTATION RATES OF MALE ADOLESCENTS AT END OF PROLONGED CONVALESCENT PERIOD AFTER ACUTE RHEUMATISM

<i>Erythrocyte Sedimentation Rate.</i>	<i>Number of Tests.</i>	<i>Percentage of ALL Results.</i>
95 or over	56	44·0
90 „	94	75·2
85 „	116	92·8
80 „	124	99·2
75 „	125	100·0

TABLE II.—TO SHOW THE HÆMATOCRIT VOLUME OF YOUNG MALE SUBJECTS (95) AT END OF PROLONGED CONVALESCENCE AFTER ACUTE RHEUMATISM

<i>Hæmatocrit Volume.</i>	<i>Number of Tests.</i>	<i>Percentage of Tests.</i>
55 and over	5	4·0
50 „	46	37·1
45 „	101	81·4
40 „	124	100·0

TABLE III.—TO SHOW THE PERCENTAGE OF POSITIVE FORMOL-GEL REACTIONS IN BLOOD SPECIMENS FROM RHEUMATIC SUBJECTS WITH HIGH, LOW AND INTERMEDIATE ERYTHROCYTE SEDIMENTATION RATES

<i>Erythrocyte Sedimentation Rate.</i>	<i>Number of Tests.</i>	<i>Positive Formol-Gel.</i>			
		<i>1 + and 2 +.</i>	<i>3 + and over 3 +.</i>	<i>Total.</i>	<i>Percentage.</i>
100-80	266	4	3	7	2·6
79-60	91	15	31	46	50·6
59-30	70	6	62	68	97·1
Total	427	25	96	121	28·3

TABLE IV.—TO SHOW THE CORRELATION BETWEEN THE ERYTHROCYTE SEDIMENTATION RATE AND FORMOL-GEL REACTION IN RHEUMATIC SUBJECTS

<i>Erythrocyte Sedimentation Rate.</i>	<i>Number of Tests.</i>	<i>Positive Formol-Gel.</i>	
		<i>Number.</i>	<i>Percentage.</i>
100-90	173	1	0.6
89-80	93	6	6.5
79-70	51	18	35.3
69-60	40	28	70.0
59-50	42	40	95.2
49-40	27	27	100.0
39-30	1	1	100.0

TABLE V.—TO SHOW THE MEAN FORMOL-GEL READING OF RHEUMATIC PLASMA GROUPED ACCORDING TO THE LEVEL OF THE ERYTHROCYTE SEDIMENTATION RATE

<i>Erythrocyte Sedimentation Rate.</i>	<i>Number of Posi- tive Formol-Gel Reactions.</i>	<i>Mean Formol- Gel Result.</i>
100-90	1	1.0
89-80	6	2.1
79-70	18	3.0
69-60	28	3.4
59-50	40	4.2
49-40	27	5.2
39-30	1	8.0

TABLE VI.—TO SHOW THE MEAN ERYTHROCYTE SEDIMENTATION RATE AND MEAN HÆMATOCRIT VOLUME OF BLOOD SPECIMENS FROM RHEUMATIC SUBJECTS GROUPED ACCORDING TO THE RESULT OF THE FORMOL-GEL TEST

<i>Formol-Gel Test.</i>		<i>Mean E.S.R.</i>	<i>Mean H.V.</i>
<i>Number.</i>	<i>Result.</i>		
9	7+ or more	46.3	38.5
14	6+	51.2	38.6
25	5+	53.8	40.3
23	4+	58.0	39.2
30	3+	66.6	42.4
28	2+ and 1+	67.9	42.7
314	Negative	86.6	44.1

TABLE VII.—TO SHOW THE PERCENTAGE OF POSITIVE FORMOL-GEL REACTIONS IN BLOOD SPECIMENS FROM RHEUMATIC SUBJECTS GROUPED ACCORDING TO THE HÆMATOCRIT VOLUME

<i>Hæmatocrit Volume.</i>	<i>Number of Tests.</i>	<i>Positive Formol-Gel.</i>	
		<i>Number.</i>	<i>Percentage.</i>
30-34	6	6	100.0
35-39	46	42	91.3
40-44	135	50	37.0
45-49	136	22	16.2
50-54	93	2	2.1
55-59	20	0	0.0
Total	436	122	

TABLE VIII.—TO SHOW THE EFFECT OF DELAY ON THE ERYTHROCYTE SEDIMENTATION RATE, AS INDICATED BY THE DIFFERENCE IN READINGS TAKEN WITHIN THREE HOURS AND AFTER TWELVE HOURS OF THE COLLECTION OF BLOOD

<i>Variation in S.R.</i>	<i>Number of Tests.</i>	<i>Percentage of Tests.</i>
1-5 increase in S.R.	42	40.0
5-10 " " " "	12	11.4
10-15 " " " "	14	13.3
15-20 " " " "	5	4.8
20-25 " " " "	3	2.9
25 or more increase in S.R. ..	5	4.8
No change in S.R.	10	9.5
1-5 decrease in S.R.	14	13.3

TABLE IX.—TO SHOW THE EFFECT OF DELAY ON THE FORMOL-GEL REACTION, AS INDICATED BY THE DIFFERENCE IN THE RESULTS OF TESTS MADE WITHIN THREE HOURS AND AFTER TWENTY-FOUR HOURS OF THE COLLECTION OF BLOOD

<i>Variation in F.G.T. Result.</i>	<i>Number of Tests.</i>	<i>Percentage.</i>
1+ increase	5	4.8
No change	85	80.9
1+ decrease	15	14.3

TABLE X.—TO SHOW COMPARATIVELY THE RESULTS OF SCHULTZ AND ROSE AND OF GREEN IN REGARD TO THE CORRELATION OF THE FORMOL-GEL REACTION WITH THE ERYTHROCYTE SEDIMENTATION TEST IN RHEUMATISM

Equivalent E.S.R. Levels.		Number of Tests at Each Level.		Positive Formol-Gel.			
				Number.		Percentage.	
Schultz.	Green.	Schultz.	Green.	Schultz.	Green.	Schultz.	Green.
100 +	0-50	36	41	13	40	36.1	97.6
70-99	51-65	24	61	16	53	66.6	86.9
40-69	66-80	42	75	25	22	59.2	29.3
20-39	81-90	63	95	23	5	38.7	5.3
10-19	91-95	44	89	7	1	15.9	1.1
0-9	96-100	66	66	2	0	3.0	0.0

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RHEUMATIC SUBCUTANEOUS . NODULE FORMATION

By F. DUDLEY HART

A WEALTH of literature has sprung up, particularly in the last few years, dealing with subcutaneous nodule formation in acute rheumatism and rheumatoid arthritis, but there is still much difference of opinion as to whether the two are closely related or whether the tissue changes are non-specific and unrelated ætiologically. As Keil (1938) writes, in a very full and comprehensive analysis of the literature on the subject, the alleged relation between rheumatic fever and rheumatoid arthritis has been adduced principally on the basis of (1) the occasional resemblances in their clinical features, including the occurrence of subcutaneous nodules; (2) the similarities in pathological changes seen in the tissues about the joints and in the subcutaneous lesions; (3) data revealed by immunological methods, which, however, are still in the early stages. There are many facts which suggest that the two conditions are of similar ætiology, but clinically the differences between the two conditions are marked, and workers have pointed out histological differences in the structure of the nodules in the two conditions (Collins, 1937).

This last author quotes the work of Massell, Mote, and Jones (1937), as does also Keil, who suggests that their work be verified using similar methods of control. These workers noted the importance of trauma in nodule formation in rheumatism, and attempted to reproduce these lesions by injections of the patient's own blood into the subcutaneous and deeper tissues of the elbow. For the next ten days the patient was instructed to rub the injected elbow on the bedclothes for some minutes six times a day. By these means they produced nodules two to three weeks later which they found clinically indistinguishable from those seen in rheumatic fever, and were thus able to study the different stages in nodule formation by histological examination after biopsy. Eighty-two patients suffering from rheumatic fever or chorea

were taken and thirty-four other non-rheumatic subjects used as controls. One elbow was injected as above, and the other was used as a second type of control. In some cases saline was injected, in others novocain with and without friction, in others friction alone, in others blood alone without friction. In the group of eighty-two patients so treated thirty-seven (45 per cent.) grew nodules, while in the thirty-four non-rheumatic controls only one developed a definite nodule, and in this case it was thought that the subject might have a rheumatic carditis. Friction alone produced no nodules in any subject, rheumatic or otherwise. Novocain in no case produced nodules, whether friction was applied or not. Injection of blood alone produced nodules occasionally, but not nearly so often as when friction was applied. Saline, however, caused nodules to grow in four patients out of twenty where whole blood in the opposite elbow had produced positive results in six cases. The authors considered that this was due to bleeding from torn vessels in the injected area, but this should presumably have also occurred to some extent with novocaine. Histologically they claimed that the lesions so produced were very similar to true rheumatic nodules, the differences lying in the infiltration of blood cells and phagocytosis present in their cases. They considered the stages of nodule formation to be very briefly: (1) alteration in the structure of the collagen with resultant oedema and deposition of fibrin-like material; (2) concurrently or immediately afterwards vascular damage with polymorphonuclear and lymphocytic infiltration and proliferation of the primitive perivascular mesenchyme and other cells, these invading the collagen foci; (3) gradual organisation, starting from perivascular areas towards the centres of the areas of necrosis; and, concurrently, (4) a typical cellular reaction—closely packed basophilic mononuclear and multinuclear cells staining like fibroblasts and apparently capable of depositing intercellular collagen. The outcome was a progressive organisation to a normal fibrous tissue replacement of the lesion. The lesions were therefore remarkably similar to rheumatic nodules, though the identity was by no means established.

The results obtained might be supposed to have been due to trauma alone and/or to actual deposition in the tissues of a nodule-forming substance present in the blood of rheumatic subjects. It would seem that—if this work be verified—here might be the basis of a study of tissue changes in

rheumatism from which fresh facts might possibly arise which would throw new light on the aetiology of the disease. We therefore attempted to reproduce this work on a group of rheumatic, rheumatoid and normal subjects. The patients were in the wards of the Royal Northern Hospital and West Wickham Heart Hospital, and may be grouped thus:

(a) Numbers 1 to 10 were over the age of thirty and suffering from rheumatoid arthritis. None had a history of rheumatic fever or chorea, none had a heart lesion. Two had sedimentation rates of under 15 mm. in one hour (micro-method, normal one to eight), eight a reading above this number. Three had subcutaneous nodules over the elbows. Eight were women, two men.

(b) Numbers 11 to 20: Active rheumatism in children under fifteen years of age. All had evidence of rheumatic carditis. Six had typical subcutaneous rheumatic nodules. In all the sedimentation rate was raised.

(c) Numbers 20 to 34: Subacute rheumatism in children under the age of fifteen years. All had passed through the acute phase, but still had raised sedimentation rates. All but one had, or had had, signs of carditis. Eight had had nodules within three months of examination which had disappeared.

(d) Numbers 34 to 50: Rheumatism in children under fifteen years with no signs of activity. Children convalescent and getting up. All had been considered to have a carditis. Sedimentation rates normal.

(e) Numbers 50 to 54: Cases of Still's disease, one inactive, three with signs of activity.

As a control a series of children suffering from other non-rheumatic conditions was used, but in only eight were injections given, as owing to the negative results in the rheumatic series this seemed to become unnecessary.

TECHNIQUE.—3 c.c. of blood was withdrawn from the median cubital vein and reinjected over the right olecranon process subcutaneously. This produced a large bulge over the point of the elbow and slightly distally, which became painless within a few minutes. The patients were instructed to massage the area vigorously several times a day with the other hand. No anaesthetic was used.

Over the left elbow 3 c.c. of normal saline was given in like manner in each case. In those cases where nodules were present over the elbows the malleoli were used or, in three cases, the

tibial processes. The latter is, however, rather an unsuitable area, but had to be used, as both elbows and malleoli were already involved in these cases.

In the first eight cases plasma alone was injected, as it was thought that this would lessen the complexity of the histology of any resulting nodule. When it was seen that there seemed to be no resultant nodule formation, this was stopped and whole blood given. The blood of four active cases actually forming nodules was injected into eight other cases—two rheumatoids, two controls, one Still's disease and three active rheumatics. Blood from one case of Still's disease and three of rheumatoid arthritis was injected into four subacute and two active rheumatic patients.

The result was entirely negative. The patients were watched for the next five weeks and no nodules of our making appeared. In two cases where we injected blood over the internal malleolus Nature provided them within a week over the external, but in no case over the experimental area. As no nodules were formed we did not feel justified in making biopsies of the tissues infiltrated.

DISCUSSION

It is difficult to explain the different results obtained by the American workers. If trauma were considered the most important factor, sufficient trauma should have been obtained in our cases, as 3 c.c. of blood raised quite a considerable hæmatoma. The total fluid injected was less by 1 c.c. in our cases, as no novocaine was given. The friction was carried out religiously in those cases under direct supervision, but it is likely that in many children the time spent on rubbing was only a few minutes a day. Nevertheless, no different results were obtained in twelve cases who were known to persevere with their exercises and were seen constantly throughout the day. It seemed that in our series of cases nodules could not be produced experimentally, though several were in a nodule-forming phase or had been so in the preceding few weeks. In five cases nodules appeared in areas other than those injected in the subsequent five weeks, so it is likely that on the law of averages we would have come across a nodule eventually in an area previously injected. Collins states that a type of fibrinoid necrosis can occur as an effect of trauma

and we have seen nodules appear in rheumatic subjects after trauma, but this seems to occur only at certain times in certain subjects and we have been unable to reproduce it experimentally.

SUMMARY

An attempt was made to reproduce rheumatic nodules by injection into rheumatic subjects over bony points of (a) the patient's whole blood, (b) whole blood from active nodule-forming cases of rheumatism, (c) separated blood plasma, (d) whole blood from rheumatoid subjects, and (e) saline, in each case friction being applied to the affected part. Four groups of patients were used: forty rheumatic (active, subacute and inactive), ten rheumatoid, four Still's disease and eight non-rheumatic subjects. No nodules were reproduced experimentally in any case, although in some cases new nodules formed elsewhere as part of the normal disease process.

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THE SOCIOLOGICAL ASPECTS OF THE TREATMENT OF ARTHRITIS

NOTES ON A VISIT TO THE UNITED STATES

By J. J. R. DUTHIE

By means of a grant made to him by the Empire Rheumatism Council the writer was enabled to spend some months in the United States studying various problems connected with the care and treatment of sufferers from the chronic rheumatic diseases. The greater part of the time was spent at the Robert Brigham Hospital, Boston. The writer would like to take this opportunity of expressing his gratitude to the members of the staff for their kindness in granting him free access to the various departments of the hospital, and also to record his appreciation of the courtesy and consideration which were shown to him at all the centres visited.

This report is concerned mainly with certain aspects of the organisation and methods of treatment in clinics for chronic rheumatic diseases which were visited.

Before any attempt is made to discuss treatment, it might serve a useful purpose to say something regarding the study of the ætiology and clinical course of the various forms of chronic arthritis. Many physicians in America believe that until sufficient knowledge is acquired of the natural course of the disease, it will not be possible to forecast with any degree of certainty the particular course which an individual case will follow. Likewise it will be impossible to assess accurately the significance of the various ætiological factors concerned or the value of any form of treatment employed. Only by studying large groups of patients over prolonged periods (throughout life if possible) can such knowledge be acquired. Such study includes details of family history, the anatomical and physiological make-up of the patient, environment, type of onset, factors believed to be of ætiological significance, the course of the disease before the patient was first examined, and a complete investigation, clinical and laboratory, which is repeated at regular intervals for as long as circumstances

permit. When a sufficiently large number of patients have been followed throughout the active phase of their disease and the data carefully analysed, it may become possible to divide cases of chronic arthritis into definite ætiological and clinical groups, and to foretell with some degree of accuracy what course the disease is likely to follow—*e.g.*, whether it will progress rapidly and result in severe incapacity early, or whether it will run a prolonged course with exacerbations and remissions. It should then be possible to distinguish the natural remissions of the disease from the remissions following various forms of treatment, or the permanent effects of some specific agent which may be discovered. A great deal of valuable work has already been carried out on this problem by Nissen, and his original papers provide illuminating reading. It is obvious that for the successful accomplishment of such a study the Rheumatic Centre must be established in the area from which the patients are drawn and not at a spa to which patients come from long distances and only stay for short periods.

SOCIAL AND HOME SERVICE

Although a great deal can be done for cases of chronic arthritis by prolonged treatment in hospital, it is too often the case that, when a patient returns to a home where conditions may be far from ideal, relapse takes place. To obtain the best results care and supervision must be extended beyond the patient's stay in hospital. On discharge the patient has to readjust himself to a mode of existence in which he has to assume a certain degree of independence and responsibility, and too often he finds himself unequal to the task. The result is that he either gives up the struggle and becomes a burden on relatives and friends or returns to hospital with an exacerbation of symptoms. In order that the transition from hospital to home may be made easier and the likelihood of relapse reduced to a minimum, physicians in American clinics have established Home and Social Service Departments whose function it is to see that everything possible is done to help the patient on his return to home and occupation. At such home service clinics patients report at regular intervals for medical and orthopædic overhaul, adjustments are made in the régime of treatment when necessary, and the patient's activities regulated and supervised. In addition, members of the social service staff pay periodic visits to the patient's home in order to

ascertain living conditions, and whether the orders of the physician in charge of the case are being carried out. Where home conditions are unfavourable, it is the duty of the social service workers to do all that lies in their power to improve them. Advice is given with regard to diet, clothing, personal hygiene, hours of rest, exercise in the fresh air, etc. In the case of a housewife, she is instructed as to how her day's work can be carried out with the minimum of fatigue, or, in certain cases where there is a young family, arrangements are made for them to be looked after elsewhere until the mother is capable of reassuming their care, or extra help is provided. Where the patient is incapable of following the régime prescribed because of financial difficulties, money is provided from whatever funds are available, charitable or otherwise. Where the occupation of a male patient is regarded as too strenuous, where surroundings at work are likely to exert a harmful influence on his disease (when work has to be done in damp, cold workrooms or shops, or outside in inclement weather, or is of such a nature as to throw undue strain on the affected joints), and where a change has been suggested by the physician in charge, it is the duty of the social service staff to enquire into all suitable alternatives and to give the patient every help in finding more congenial employment. When patients are unable to come to the home service clinic, the home visitor reports to the physician regarding their progress, and, should this be unsatisfactory, arrangements are made to have the patient brought back to hospital for a day or two, when the situation can be reviewed and the necessary measures adopted. At any arthritis clinic a certain number of patients will present themselves who are unsuitable for treatment for one reason or another—*e.g.*, because of a hopeless degree of crippling or because of organic visceral disease. The Social Service Department takes care of such patients and arranges for their disposal.

For the running of such a department a highly trained staff is essential. At American colleges courses in social service work are available, and young women are trained for this branch of medical work. The courses include instruction in the effect of environment on disease, in dietetics, in housing conditions, etc. Arthritis clinics also function as teaching units, where practical instruction is given to college students training for social service work. Volunteer workers undertake many of the duties which do not require special training, such as arranging

for financial aid where necessary, and seeing that the patient is receiving proper care at home.

Anyone who has been associated with the treatment of chronic arthritis will know only too well how prone the patients are to give up the struggle to get well as soon as the care and encouragement of doctor and hospital staff are removed. When assurance is given that care and treatment will be carried on by the home service staff, and that everything will be done to overcome the various problems which have to be faced on the resumption of an active existence, the transition from hospital to home is rendered much more agreeable, the maximum benefit can be derived from a stay in hospital, and the tendency to relapse reduced to a minimum. In actual fact the duration of hospitalisation may be materially shortened because there is no danger of a serious breakdown occurring without the knowledge of the physician in whose care the patient has been. In the writer's opinion, the establishment of such departments at all arthritis clinics would greatly increase their efficiency, and would amply justify the additional outlay entailed.

OCCUPATIONAL THERAPY IN THE TREATMENT OF CHRONIC ARTHRITIS

One of the most difficult aspects of the treatment of chronic arthritis of the rheumatoid type is the rehabilitation of the patient once the active stage of the disease has passed. Even when treatment has been instituted early in the disease and deformities have been prevented, the patients are left with varying degrees of muscular weakness. Carefully prescribed exercises may do a great deal to restore muscular tone and power, but the re-education of the patient in the co-ordinated use of various groups of muscles requires something more. Occupational therapy is used for this purpose in American clinics, and the excellent results obtained more than justify the expenditure required to establish departments with trained personnel. Its value in other diseases is well recognised in this country, but its use in the treatment of chronic arthritis appears to have been somewhat neglected. Occupational therapy, in addition to re-educating the patient in the use of the limbs, supplies a mental stimulus of great psychological value. The fact that the work undertaken has a definite object in view results in the patient's interest being

aroused, and his thoughts are occupied to the exclusion of morbid brooding on his physical disability. This promotes a healthier state of mind, and acts as an added incentive to get well.

In addition to being a valuable form of treatment, occupational therapy may be a means whereby a patient who cannot return to his former occupation may be enabled to earn a livelihood, or at least to contribute something towards the cost of his care. The money from the sale of goods manufactured by patients may be used to defray the cost of running the occupational therapy department, which can also function as a teaching unit for students, whose fees form another source of income.

In a high proportion of cases of rheumatoid arthritis the greatest disability results from deformities of the wrists, hands and fingers. In many instances the degree of deformity present is so marked that any return of useful function seems impossible, but it is truly remarkable how a course of occupational therapy under skilled supervision may enable the patient to perform highly specialised work, and to produce articles of real artistic merit. Examples of suitable occupations for such cases are weaving, basket making, leather work, painting, rug making and metal work. In cases where the elbows and shoulders are also involved the controls of a hand loom can be adjusted to secure any degree of motion desired in the affected joints. As improvement occurs, greater ranges of movement can be obtained by further adjustments. It is not necessary to wait until the patient is ambulatory before occupational therapy is started. Many types of work can be performed in bed or chair. When the patient is considered fit to resume walking, a preparatory course of work at a loom with foot controls or at a fretwork saw driven by a treadle or pedals will do a great deal to strengthen the legs before actual weight-bearing is begun.

In all forms of occupational therapy it is essential to arrange the work so that the patient maintains a good postural position while engaged in it. Much harm may result from allowing a patient to slouch over a bench or to sit hunched up in bed. Short-sighted patients should not be given fine work which will tend to make them assume a stooping position.

The writer was greatly impressed by the beneficial effects of such therapy and by its wide application in the treatment of the chronic rheumatic diseases.

MEDICAL AND ORTHOPÆDIC CO-OPERATION IN THE
TREATMENT OF CHRONIC ARTHRITIS

Many of the problems to be faced in the treatment of chronic arthritis are orthopædic in nature. A thorough knowledge of orthopædic principles is necessary for the management both of the early stages of rheumatoid arthritis, when the object is to prevent deformity, and of the later stages, when it is necessary to correct established deformities. It occurs not infrequently that an orthopædic surgeon is called upon to perform an operation for the correction of a deformity which should never have arisen. On the other hand, a patient may be submitted to a major surgical operation when his general condition renders him totally unfit for such a procedure. Only by the closest co-operation between physician and surgeon can such disasters be avoided.

In the Robert Brigham Hospital, Boston, the medical and orthopædic staff share equally the responsibility of deciding what lines of treatment are to be adopted in each case. Every patient is seen at frequent intervals by the physician and surgeon. The problems of the individual case are discussed and measures are adopted which are calculated to produce the best results from both a medical and surgical point of view. For example, if it is decided that an operation is necessary to correct an established deformity, it is the duty of the physician to ensure that the patient is in the best possible condition before it is performed. Great emphasis is laid on this pre-operative period of preparation. It is claimed that post-operative results more than justify the delay. Not only is treatment directed towards improving the patient's general health, but by carefully planned exercises postural faults are corrected and the tone of the body musculature is improved. As a result, after the operation has been performed the patient is in the best possible condition to undertake the often arduous task of reclaiming the function of a joint long disused. The physician, in addition to attending to the physical condition in the pre-operative period, must also discover the patient's attitude of mind towards the operation and towards recovery in general. Many chronic arthritics who, on account of disability, have been confined to bed for long periods become apathetic. They no longer desire to return to active life, with its accompanying responsibilities. Such patients are regarded as very poor material from the surgical point of view, because,

no matter how successful the operation may be in securing a mechanically perfect result, the functional result may be negligible. Before any operative procedure is decided upon, both physician and surgeon must be satisfied that the patient understands what the operation means to him and his full co-operation secured. If the patient has lost the wish to get better, and where pre-operative psychotherapy fails to reanimate this desire, surgical interference is not advised.

The collaboration between physician and surgeon does not end with the patient's discharge from hospital. A member of the orthopædic staff is in attendance at the home service clinic, where all patients report at regular intervals. If, after an operation, a patient has been discharged with a supportive apparatus, such as a walking caliper or knee cage, adjustments soon become necessary, and these are carried out under the surgeon's supervision, and he also decides when the apparatus is to be discarded. At the same time the physician examines the patient and adjusts the medical régime as the need arises.

As a result of this close association of the physician and orthopædic surgeon in the treatment of patients during and after their stay in hospital, a surprisingly high proportion of cases of chronic arthritis return to active occupations and become wholly or partially self-supporting.

THE ORGANISATION OF AN ARTHRITIS UNIT

While visiting centres for the treatment of chronic rheumatic disease in America, the writer was impressed by the efficient manner in which these units were organised. The impression created at first was that much larger staffs are employed than is the case in an institution in this country with a similar number of beds. Closer study revealed that each member of the staff was fulfilling a function which was regarded as essential to the study and successful treatment of chronic rheumatic disease. The number and diversity of the services required is a striking commentary on the complexity of the problems involved. For the investigation of cases all the routine services must be available—radiological, biochemical, bacteriological, etc.—and, if the unit is to be independent of any other institution, the cost of supplying these facilities constitutes a serious obstacle to the establishment of new centres. The most obvious solution to this problem is that centres should be organised in connection with general

hospitals where such services are already available. In American clinics there are laboratories where special investigations can be carried out, and where ætiological problems are studied. It is only by providing such facilities that the best use can be made of the material, clinical, pathological and biochemical.

A rheumatism clinic should be equipped to treat both out-patients and in-patients. No limit should be imposed on the length of time that a patient may occupy a bed. The majority of cases require at least two to three months in hospital (the average stay of patients in the Robert Brigham Hospital, Boston, was two months six days), and some cases require much longer. As a result, the number of in-patients treated in a given period may appear relatively small in comparison with the number treated in the wards of a general hospital, but in organising a treatment centre the policy of adequate and prolonged treatment of the individual case should be strictly adhered to, as only thus will satisfactory, permanent results be obtained.

As has already been emphasised, a vitally important part of the work of the unit is the treatment and supervision of patients after their discharge; therefore, in planning the various departments (occupational therapy, physiotherapy, hydrotherapy) it must be borne in mind that the majority of in-patients will continue after discharge to attend the clinic for treatment, and provision must be made accordingly with regard to staff and equipment, as the number of such patients will become progressively larger the longer the clinic has been in existence.

Many sufferers from the less serious forms of rheumatic disease can be treated adequately as out-patients, and accommodation for examination of such patients should not be forgotten.

The successful treatment of chronic rheumatic disease depends far more on the skill of the physician in charge and his assistants than it does on various forms of treatment requiring complicated and expensive apparatus, and where funds are limited money is best spent on the provision of properly trained personnel. A great deal can be done with relatively simple equipment if treatment is in the hands of a skilled staff. This is well illustrated in certain American clinics where there is a surprising absence of many forms of apparatus which have come to be regarded as essential fittings in any physiotherapeutic department.

In conclusion a word might be said regarding the maintenance of case records. The writer was bewildered by the number of

different systems employed in the various hospitals and clinics visited. Such diversity of method renders it exceedingly difficult to compare the records of one clinic with those of another, and many valuable data, which might otherwise become available, are lost. The adoption of a standard method of recording history, clinical findings, results of special investigations, progress notes, and follow-up notes would greatly facilitate the comparison and analysis of the records of different clinics. By this means information regarding the ætiology, pathology and clinical course of large numbers of patients suffering from the different types of the chronic rheumatic diseases would become available.

JUVENILE RHEUMATISM IN LONDON

By FRANCIS BACH, N. GRAY HILL, T. WARWICK PRESTON
AND CHARLES E. THORNTON

FOR the purpose of this paper it is to be understood that the term "juvenile rheumatism" refers to rheumatic disease occurring in children under the age of sixteen. This definition is convenient rather than scientific. It is convenient clinically, in that by far the greater number of initial attacks occur before the age of sixteen, and it has the further practical convenience that up to this age children come within the scope of the provisions of the Education Acts, whereby special facilities are available for treatment and supervision. Nevertheless it must be borne in mind that rheumatism of the juvenile type does occur in individuals above the age of sixteen, and that rheumatoid types of the disease resembling those found in adults sometimes occur in children. It should also be understood that the authors have restricted themselves to summarising facts connected with the clinical and sociological aspects of the disease; no attempt has been made to discuss or summarise the results of recent bacteriological or biochemical research. Though this work has revealed interesting and suggestive facts, further progress must be made before they can be applied by the clinician or influence the public health administrator in his endeavours to reduce the incidence or minimise the direful effects of juvenile rheumatism.

For practical purposes juvenile rheumatism may be classified according to its manifestations into:

- (a) Acute rheumatic "fever," usually involving the joints.
- (b) Subacute rheumatism involving the joints, muscles, and fibrous tissues.
- (c) Acute rheumatic carditis and/or pericarditis.
- (d) Insidious carditis developing with or without evidence of associated peripheral rheumatism.
- (e) Chorea.

All these forms of the disease, although differing widely in some respects, exhibit two tendencies in common—a tendency to recur repeatedly and a tendency to cause permanent cardiac

damage. Furthermore, a combination of one or more of these manifestations may, and often does, occur in the same child.

It cannot be too strongly emphasised that acute rheumatism with its swollen joints, the muscle and joint pains and fatigue syndromes of childhood, the chorea of childhood, and the acquired forms of heart disease are all manifestations of the same systemic disease, which may run a course extending over a period of many years. It is indeed but too true that, in the words of Cheadle, "the history of rheumatism may be the history of a whole childhood," and he might have gone even further and said "the history of a whole life."

INCIDENCE OF JUVENILE RHEUMATISM IN LONDON

Juvenile rheumatism in its various guises, together with its cardiac sequelæ, is the most common single cause of persistently irregular school attendance. The returns of the school attendance department of the London County Council for 1936 showed that of children out of school for three months or more on account of illness, the rheumatic diseases accounted for 26·7 per cent. of the total number. Again, rheumatic children form about one-half of the total number of children in attendance at schools for the physically defective. Medical supervision and treatment and the provision of special education for the rheumatic children of London involves an annual charge on public funds of approximately £200,000, and about 20 per cent. of rheumatic children have suffered a degree of cardiac damage which renders them unfit, on leaving school, to undertake any but the lightest of occupations.

ESTIMATED NUMBER OF RHEUMATIC CHILDREN IN LONDON

To estimate the actual number of children in London suffering from rheumatic infection or its sequelæ is not easy. The following figures are in the nature of an approximation. The actual number of rheumatic children is undoubtedly considerably greater than the total here obtained.

NUMBER OF RHEUMATIC CHILDREN UNDER SUPERVISION OR TREATMENT, JUNE, 1938

Number under supervision by school doctors	2,632
Number under supervision at supervisory centres	5,160
Number under treatment in the Council's rheumatism units	872
Total	8,664

This total represents the number of "active" or recently active cases of juvenile rheumatism. It does not include a very large proportion of rheumatic children between fourteen and sixteen years of age who have left school; neither does it include a large number of children still at school who have been discharged, for the time being at least, from supervision. A better idea of the real extent of the prevalence of the disease is obtained from the number of children whose records are found in the card index kept in the Public Health Department. In June, 1938, this number was 22,800. All these children are known to have suffered or to be suffering from rheumatic infection. The estimated child population of London—*i.e.*, children up to the age of fifteen—was in 1935 approximately 878,000, and it is tending to diminish. Taking, however, this figure of 878,000, 22,800 rheumatic children represents an incidence of rheumatism in approximately 2.6 per cent. of the child population.

INCREASE OR DECREASE IN THE OCCURRENCE OF JUVENILE RHEUMATISM

At present it is difficult to be sure whether or not any diminution in the prevalence of juvenile rheumatism is occurring. During the last ten years greatly increased provision has been made in London for the treatment and supervision of rheumatic children, and it is certain that the yearly increase during this period in the number of children referred for treatment under the London County Council's Rheumatism Scheme is more a reflection of the increased provision made than an indication of an increasing prevalence. Indeed, there are signs that no notable increase is occurring. About the middle of 1935 the scheme was reviewed and additional beds provided in the special hospitals in numbers sufficient, it was estimated, to meet all demands. The experience of the last three years shows that the number provided is adequate approximately to present needs. The number of applications received for admission to these special "rheumatism units" has shown a tendency to become stabilised at about 2,000 to 2,500 per annum.

CHANGE IN TYPE

It is of importance to ascertain, if possible, if any evidence exists tending to indicate a decreasing virulence of the disease either in connection with its acute phases or with regard to the

incidence and severity of its cardiac complications. If such a decrease in virulence can be shown to be occurring, it is a fact hardly less in importance than an actual decrease in the general incidence of the disease. In so far as the acute phases are concerned, all clinicians agree that the type of case characterised by acutely swollen joints, sour sweats, and severe prostration is now rarely seen. This change of type has no doubt been brought about partly by earlier and more intensive treatment in the acute stage, and in part is due to a gradual increase in the disease-resisting power of the child population. For this latter factor improved social conditions and careful medical supervision during school life are chiefly responsible. It would, however, afford little ground for satisfaction if, associated with this decrease in severity of acute rheumatism, there was no corresponding decrease in the amount of rheumatic heart disease. Whether a child suddenly becomes a cardiac cripple following an attack of acute rheumatism or chorea, or gradually becomes a cardiac cripple following a milder subacute attack, the result is equally disastrous. The medical inspection of school children, by revealing the presence of an enormous amount of unsuspected rheumatic cardiac disease, showed that the milder types of rheumatic disease were likely to be no less inimical to the prospects of a useful and prolonged life than were the more acute types of attack which formerly were common. The percentage of children found by the school doctors to be suffering from rheumatic heart disease has, however, decreased from 2.0 per cent. in 1926 to 0.77 per cent. in 1937. It can therefore be asserted with a certain degree of confidence that even if there be no notable decrease in the incidence of rheumatic infection, there has been a definite decrease both in the virulence of the acute form of the disease and in the frequency and severity of the cardiac complications.

ONSET AGE OF JUVENILE RHEUMATISM AND CHOREA

An analysis was made of 1,000 cases admitted to the Council's rheumatism units during the first six months of 1937. The greatest care was taken to ascertain the age at onset of the initial attack. Diagram 1 shows:

- (a) Age at onset of all cases (both sexes).
- (b) Age at onset of muscular or articular rheumatism (both sexes).
- (c) Age at onset of chorea (both sexes).

In general the graphs indicate that quite an appreciable number of cases of juvenile rheumatism occur in children under the age of five, and that there is a gradually increasing susceptibility up to the age of nine in the case of chorea, and up to the age of eleven in the case of articular or muscular rheumatism. It is, however, exceedingly rare to find cases in which the onset

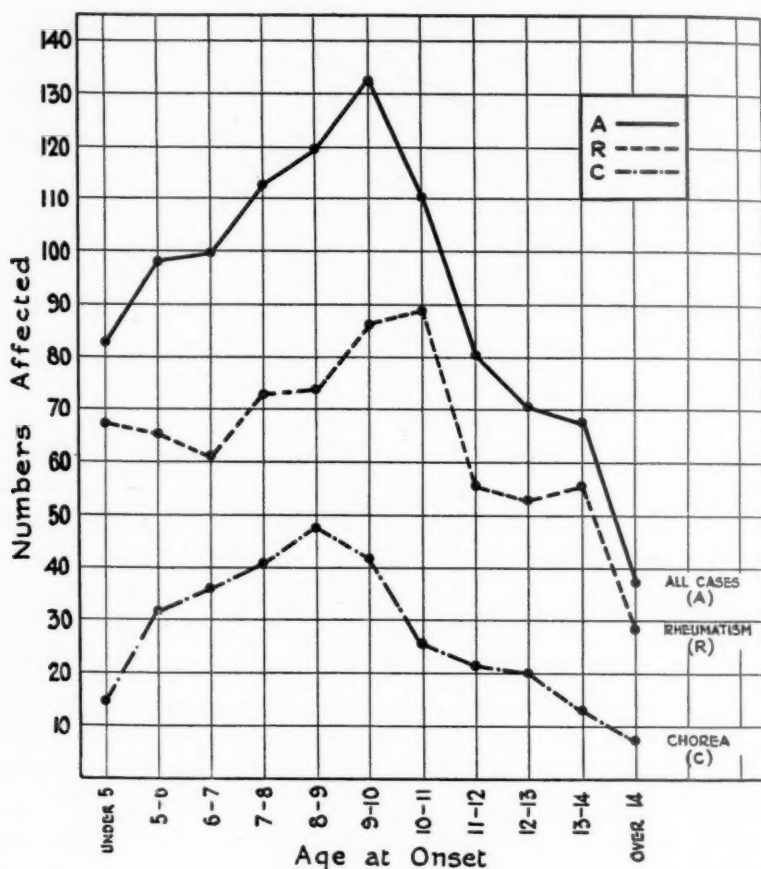


DIAGRAM 1.—SHOWING AGES AT ONSET IN 1,000 CASES OF RHEUMATISM AND CHOREA.

occurred in children below the age of three. After the age of eleven it would seem that susceptibility to both diseases rapidly diminishes until at the age of fourteen the "risk" appears to be only about half what it was at the age of five. The dangerous age for children in regard to rheumatic infections lies between five and twelve years.

INFLUENCE OF AGE INCIDENCE ON PROGNOSIS

An attempt was made to discover if the age at onset of rheumatic infection had any influence on the prognosis of the disease. With this object in view the authors endeavoured to trace the after-histories of two series of cases. The first series of 200 was taken from children treated in the rheumatism unit at Queen Mary's Hospital during 1927; the second series from children treated in 1932. Unfortunately it was only possible to trace in the two series together a total of 242 children. This relatively small proportion traced reduces the validity of deductions made therefrom, but the results are nevertheless interesting. As the numbers are small the two series have been tabulated together.

TABLE I.—CONDITION IN 1937 OF 242 PATIENTS TREATED AT QUEEN MARY'S (L.C.C.) HOSPITAL IN 1927 AND 1932

Age Classification.	Alive and Well.			Invalid.			Deceased.		
	Boys.	Girls.	Total.	Boys.	Girls.	Total.	Boys.	Girls.	Total.
Aged 5 years and under ..	8	10	18	2	10	12	1	3	4
Aged 6-9 years ..	22	30	52	4	19	23	8	13	21
Aged 9-12 years ..	17	32	49	2	8	10	4	5	9
Over 12 years ..	10	16	26	1	4	5	4	2	6
Age at onset unknown ..	—	3	3	—	1	1	—	3	3
Totals ..	57	91	148	9	42	51	17	26	43

It would appear that those who are attacked by rheumatism during the early years of school life fare the worst. The numbers of children studied are too small to allow any definite conclusions to be drawn, but it would seem that the chances of cardiac damage diminish as the heart takes on the more adult form. As is shown in the table, there are 130 children *under* nine years of age who were treated, and at the time of this investigation sixty of these were either dead or invalided, leaving only seventy to be classed as alive and well. On the other hand, of the 105 children *over* nine years of age only thirty are dead or invalided and seventy-five are known to be enjoying good health. The earlier the age of onset, the worse would seem the prognosis for the rheumatic child.

SEX INCIDENCE

The greater susceptibility of girls to rheumatic infection is universally recognised. All collected statistics are in agreement on this point. The relative number of boys and girls admitted during 1934, 1935 and 1936 to the rheumatism units of the London County Council may be quoted.

Number of boys admitted	2,069
Number of girls admitted	2,705

Using these figures, the ratio of the number of boys affected to the number of girls is almost exactly 3 : 4.

An analysis of 3,683 children attending rheumatism supervisory centres gave a similar result.

Percentage of boys under supervision	41.7
Percentage of girls under supervision	58.3

These figures indicate the ratio of boys affected to girls affected as being equivalent to 3 : 4.2—a ratio which is in close agreement with that obtained from the hospital figures.

SEX INCIDENCE RELATED TO TYPE OF CASE

The preponderance of girls affected was greatest in the milder type of case—i.e., cases of persistent subacute rheumatic pains with no definite cardiac involvement. This is shown by the following figures taken from statistics of the supervisory centres:

TABLE II.—SEX INCIDENCE OF THE VARIOUS TYPES OF CASE

Sex.		<i>Cases with History of Acute Arthritis.</i>	<i>Cases of Definite Chorea.</i>	<i>Cases of Acquired Cardiac Disease, but with no Definite Rheumatic History.</i>	<i>Mild Subacute Rheumatism or Chorea without Cardiac Involvement.</i>
Boys	..	42.8 per cent.	42.8 per cent.	46.0 per cent.	39.0 per cent.
Girls	..	57.2 „	57.2 „	54.0 „	61.0 „

INFLUENCE OF SEX ON THE INCIDENCE OF CARDIAC INVOLVEMENT

Considering the sexes separately, it is found that cardiac involvement occurs slightly more frequently in boys than in girls. In the previously quoted 4,774 admissions to rheumatism units,

of the boys 40.2 per cent. had signs of cardiac involvement, whilst in only 37.4 per cent. of the girls was the heart affected. Similarly, when discharged from hospital *permanent* cardiac damage is found more frequently in boys than in girls. An analysis of 1,152 cases discharged showed that in boys the heart had become permanently damaged in 38 per cent. of cases. Only 33.3 per cent. of the girls were similarly affected. Two possible explanations of this preponderance of cardiac involvement in boys may be advanced. The first suggests that it is correlated with the somewhat greater physical activity which boys exhibit, and their disinclination to accept the rôle of invalid until compelled to do so. Alternatively, it may be that the greater incidence of cardiac involvement in boys is related to their apparently greater susceptibility to rheumatic infection between the ages of six and seven. It has already been pointed out that the earlier the age of onset, the greater the risk of cardiac damage. Possibly both explanations may be to a certain extent true.

While in hospital more boys than girls die of cardiac failure, and this fact has been quoted as indicating that a more severe type of carditis occurs in the young male. When, however, a follow-up investigation was carried out, there was no appreciable difference found in the mortality figures for the two sexes, and, moreover, the invalidity figures for girls were appreciably higher than in the case of boys.

THE RELATIONSHIP OF JUVENILE RHEUMATISM TO SOCIAL ENVIRONMENT

It is commonly held that rheumatism is a disease of the children of the poor and is comparatively rarely met with amongst the children of the more prosperous classes. *A priori* it is reasonable to suppose that this is likely to be true. If, as is at least probable, the disease is due to an infection, it should naturally occur most frequently amongst the children of the poor, living as they often do under conditions of overcrowding, sometimes in damp tenements or basement dwellings.

Such unfavourable surroundings, possibly in a proportion of cases associated with insufficient or improper food, will obviously tend to render children a more easy prey to any form of infection, and, once infected, render the outlook more unfavourable.

DIFFICULTIES IN THE OBTAINING OF RELIABLE STATISTICS

When, however, an attempt is made to evaluate this preponderance (assuming it exists) difficulties at once arise. Rheumatism is not (except in a negligible number of districts) "notifiable." Indeed, it is a difficult disease to include in any Notification Act, owing to the indefinite character of many of its manifestations. Consequently, our knowledge of its prevalence is in the main obtained by the analysis of hospital statistics or the statistics of the school medical services. Deductions from hospital statistics always tend to be vitiated by the fact that the information obtained relates in the main to those who are in the habit of relying on hospitals for medical treatment—*i.e.*, the poorer classes of the community; in these statistics the poor always preponderate. This is particularly the case where the milder forms of rheumatism are concerned. The poor take their children to the hospital out-patient department or rheumatism supervisory centre; the more prosperous seek the advice of their family doctor. Since for detailed information we are almost entirely dependent on these hospital and supervisory centre statistics, it follows that in one section of the community almost every case of juvenile rheumatism is noted and supervised, whilst for the more prosperous classes we have only very scanty information. The above points must be remembered in considering how much light is thrown on the question by the subjoined figures:

TABLE III.—HOME ENVIRONMENT OF 1,000 CHILDREN ADMITTED TO THE COUNCIL'S RHEUMATISM UNITS, JANUARY TO JUNE, 1937

<i>Disease.</i>		<i>Percentage of Homes classed as Very Good.</i>	<i>Percentage classed as Average.</i>	<i>Percentage classed as "Poor."</i>
Rheumatism	..	1.0	55.2	14.0
Chorea	..	0.4	23.4	6.0
Totals	..	1.4	78.6	20.0

The table shows that 20 per cent. of rheumatic children came from very poor homes, but, on the other hand, it is quite possible that if careful enquiry were made into the home environment of 1,000 non-rheumatic children from the same

social class, practically the same percentage of unsatisfactory conditions would be found. More significant, perhaps, is the fact that in only 1.4 per cent. of the children could the homes be classified as "very good," but here again the warning as to the possibility of rheumatic children who live in very good homes being privately treated, and thus not appearing in these figures, must be remembered.

Cases in which there was evidence of rheumatism being brought on by gross neglect, etc., were extremely few.

With a view to ascertaining if a bad home environment had an unfavourable influence in connection with the supervision of cardiac complications or the occurrence of relapses, an analysis was made of 1,500 admissions to rheumatism units. The results (see Table IV.) seem to show that rheumatic children coming from damp or overcrowded homes run no greater risk, so far as cardiac involvement is concerned, than do children more fortunately situated; neither is the slightly greater percentage of recurrences which they exhibit large enough to be significant.

TABLE IV.—HOME ENVIRONMENT OF RHEUMATIC CHILDREN AND ITS RELATION TO CARDIAC COMPLICATIONS AND RELAPSES (1,500 CASES)

<i>Type of Dwelling.</i>	<i>Number of Children.</i>	<i>Cardiac Involvement.</i>		<i>Relapses.</i>	
		<i>Number.</i>	<i>Percentage.</i>	<i>Number.</i>	<i>Percentage.</i>
Average	959	416	43	474	49
Damp	206	83	40	113	54
Overcrowded ..	246	108	44	138	56
Damp and overcrowded	89	38	42	47	53
Totals	1,500	645	43	772	51

DISTRIBUTION OF JUVENILE RHEUMATISM IN LONDON

The distribution, as indicated by the number of nominations for institutional treatment per 1,000 elementary school children in the various London boroughs, seems to coincide fairly closely with density of population, and therefore is, in the main, heaviest in the poorer and more overcrowded boroughs. In general, the heaviest incidence falls on the boroughs immediately adjoining the south bank of the Thames. These are densely populated areas, and perhaps their situation on the river flood-plain has

a contributory influence. Wandsworth on the west and Greenwich and Woolwich on the east exhibit a lower incidence, and in these boroughs the population density per acre is considerably less. On the north side of the Thames the greatest incidence falls on Finsbury, Shoreditch, Bethnal Green, Stepney and Stoke Newington—all densely populated areas.

SEASONAL INCIDENCE OF JUVENILE RHEUMATISM

Juvenile rheumatism exhibits a very definite seasonal incidence. An analysis of the months of onset of 1,500 cases admitted to the rheumatism units during 1935 showed the disease to be most prevalent during the period October to February—i.e., during the coldest, darkest and most humid months of the year. A definite relationship would appear to exist between the prevalence of rheumatism and the amount of sunshine, the mean air temperature and the percentage atmospheric humidity. A low mean air temperature, a small amount of sunshine and a high percentage of humidity, when occurring simultaneously, seem to be associated with a high incidence of rheumatic infection. Conversely, plentiful sunshine combined with a high mean temperature and low humidity are associated with a very obvious fall in the number of rheumatic cases. These facts are shown graphically in Diagram 2.

MODES OF ONSET OF RHEUMATISM AND CHOREA

The following figures show the modes of onset in 1,000 cases admitted to the rheumatism units during the first half of 1937:

TABLE V.—MODES OF ONSET OF RHEUMATISM AND CHOREA
(1,000 CASES)

<i>Mode of Onset.</i>	<i>Rheumatism, Acute and Subacute.</i>	<i>Chorea.</i>	<i>Total.</i>
Spontaneous	621	257	878
Following "chills" (tonsillitis usually)	47	3	50
Following scarlatina	15	6	21
Associated with "bathing"	3	—	3
Associated with wet clothing	7	1	8
Following tonsillectomy	7	6	13
Following "accidents"	1	10	11
Following a "fright"	3	9	12
Associated with school work	—	4	4
Totals	704	296	1,000

The great majority of cases of rheumatism appear to have a "spontaneous" onset. In acute cases the parent usually

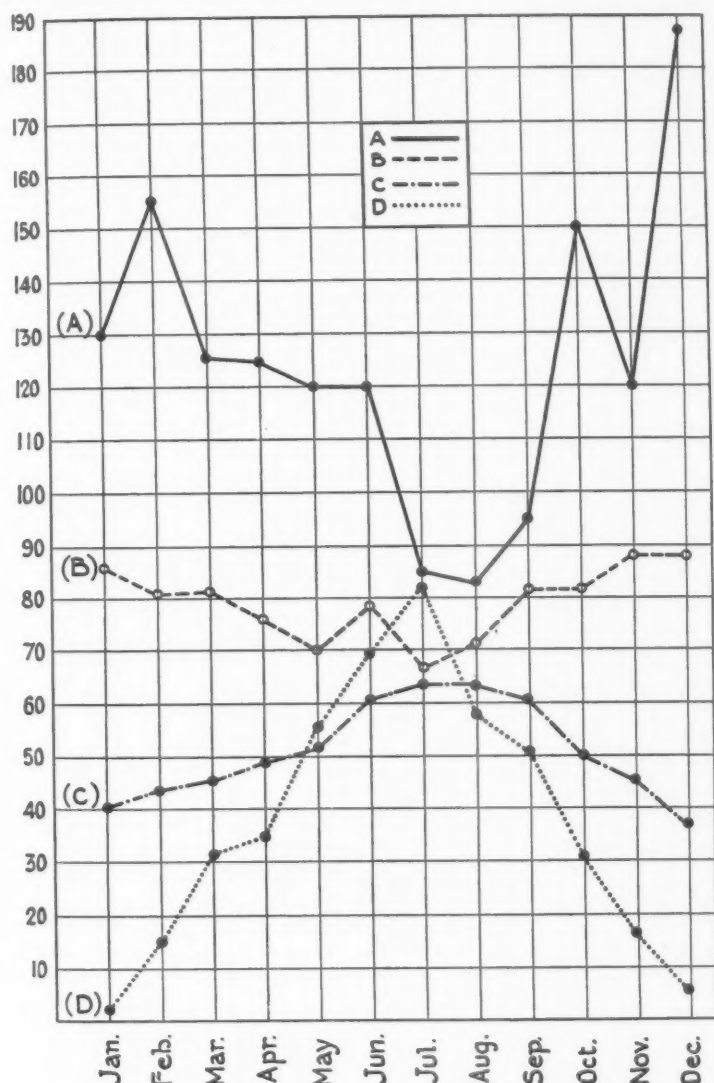


DIAGRAM 2.—SEASONAL INCIDENCE OF JUVENILE RHEUMATISM.

(A) Months of onset of 1,500 cases of rheumatic infection (including chorea). (B) Monthly percentage of atmospheric humidity. (C) Mean monthly air temperature. (D) Average number of hours of sunshine per day each month multiplied by 10.

asserts that the child was quite well prior to the attack. In a small proportion of cases the attack is ascribed to a "chill,"

which, on enquiry, is usually found to have been an attack of tonsillitis. The number of cases attributed to bathing, paddling or wet clothing is almost negligible.

TRAUMA, SCHOOL WORK AND CHOREA

Special enquiries were made in cases of children suffering from chorea as to the possible association of the attack with mental or physical "shock" or with school work. The figures given in the above table show that in twenty-five instances (*i.e.*, in almost exactly 8 per cent.) the attack was associated with mental or physical trauma.

It has often been suspected that attacks of chorea in children may be induced by school work or the strain of preparing for examinations. There is little direct evidence to support this view. Of the 296 cases analysed, in only four cases was the attack attributed to school work. In twenty-two cases found in secondary school children, the cause in four instances was asserted to be "worry" regarding examinations. This is a high proportion, but, on the other hand, the small total number of cases of chorea found suggests that the incidence of chorea in secondary school children is particularly low.

RHEUMATIC PAINS

A detailed analysis made by Dr. T. W. Preston of 257 rheumatic children attending his supervisory centres led him to the following conclusions, which are of special interest in connection with insidious carditis and complaints of rheumatic pains:

(i) Whereas a long history of aching limbs is common in children who show nothing objective, on the other hand children with severe rheumatic carditis often make but little complaint of pain.

TABLE VI

	<i>Cases of Carditis.</i>	<i>Insidious Rheumatism without Carditis.</i>	<i>Doubtful Rheumatism.</i>
Constant complaints ..	—	7 per cent.	6 per cent.
Fairly frequent complaints ..	10 per cent.	50 "	48 "
Infrequent complaints ..	32 "	43 "	46 "
No complaints ..	58 "	—	—

Similar observations were made in a previous investigation; then it was also noted that frequent complaints of aching limbs were uncommon in children with a former history of acute rheumatism.

(ii) The development of carditis in the whining child who, according to the mother, has had rheumatism "all its life" seems to be extremely rare.

(iii) The more carefully one investigates the histories of cases of "insidious carditis," the fewer become the cases which are truly "insidious." If one classes a case as "insidious" merely because the parent says that the child has never had acute rheumatism or chorea, the number will be large; but on close enquiry many of these will be found to have had a mild illness which was undoubtedly subacute rheumatism.

(iv) The sudden development of a stiff joint in a child is extremely likely to be rheumatism; some of these cases have masqueraded as "sprains," and this diagnosis should not be accepted in the absence of a convincing history of trauma.

(v) Unfortunately, in the absence of a reliable biochemical or serological test there is no definite means of diagnosing rheumatism with certainty, and it is necessary to take a cautious attitude with a child complaining of aching limbs. After a careful examination, however, and a reasonable period of observation, there would seem to be no sound reason for advising a life of semi-invalidism merely on account of "growing pains."

TREATMENT OF JUVENILE RHEUMATISM: THE LONDON COUNTY COUNCIL'S RHEUMATISM SCHEME

In London the beginning of an organised effort to combat the menace of juvenile rheumatism dates from the latter end of 1926, when a special unit of sixty beds was established by the Metropolitan Asylums Board at Queen Mary's Hospital, Carshalton. For several years a feeling had been steadily growing that a disease which, clinically, in its smouldering course much resembled tuberculosis should be dealt with on similar lines—i.e., by early and prolonged rest followed by a period of close supervision. Although administrative action had been taken with regard to tuberculosis as early as 1908, interest in the problem of rheumatism in children was not really aroused (although a good deal of pioneer work had been done in America) until about 1923, when the question was discussed at the annual meeting of the British Medical Association. Following this, Sir George Newman, in his annual report to the Board of Education for 1924, and the Invalid Children's Aid Association, in a memorandum in 1925, urged the necessity for the provision of more institutional accommodation for rheumatic children—where it

would be possible to continue the child's education during the latter part of its enforced stay in hospital.

A comprehensive scheme was therefore organised, under the direction of Dr. C. J. Thomas, one of the Council's Senior Medical Officers, for the treatment and supervision of rheumatic children under the age of sixteen, having in view:

(a) A gradual increase in the accommodation in special rheumatism units until beds in sufficient number were available to provide for an average period of treatment of six months for all children showing signs of active disease.

(b) The establishment of Rheumatism Supervisory Centres for the purpose of early diagnosis of doubtful cases and supervision of quiescent cases.

(c) The establishment of an alternative system of supervision by the school doctors.

(d) Investigation and amelioration, if necessary and possible, of the child's home environment.

(e) The central co-ordination of the various branches of the scheme.

(a) **THE SPECIAL RHEUMATISM UNITS.**—The present accommodation available amounts to 650 beds for acute and subacute cases, with an additional 250 for doubtful or extremely mild cases or cases of rheumatic heart disease in which a short period of convalescence for the purpose of cardiac rest is desirable.

These rheumatism "units" (with one exception) are recognised by the Board of Education as "hospital schools," and are staffed by qualified teachers.

(b) **ESTABLISHMENT OF RHEUMATISM SUPERVISORY CENTRES.**—The provision of such centres was agreed to by the London County Council in February, 1928, and a few weeks later the first two centres were opened. This number was quickly increased, until at the present time twenty-one such centres are in existence, and in December, 1938, 5,160 children were under supervision.

The purpose of these centres is:

(i) To keep under periodical medical supervision children known to have suffered from an attack of any form of rheumatic infection.

(ii) To keep under observation children suffering from mild rheumatic symptoms and to advise parents as to the general care of such children.

(iii) To advise parents, teachers and others concerned of any special modifications which are desirable in connection with the

education of the rheumatic child—*e.g.*, recommendations regarding restriction of physical exercises, playground activities or "homework" may be made; or it may be advised that a transfer to a school for physically defective children is desirable.

(iv) To ascertain the home conditions of children attending the centre, and to take such action as may be necessary or possible to improve an unfavourable environment.

(v) To act in a specialist advisory capacity to school doctors and others who may refer doubtful cases for diagnosis.

In particular it is to be noted that the Rheumatism Supervisory Centre, as its name implies, is not a centre for treatment; its functions are supervisory and advisory.

(c) SUPERVISION BY THE SCHOOL MEDICAL SERVICE.—In many instances supervision at the Rheumatism Supervisory Centres is considered either not necessary or not desirable. For such cases arrangements are made for the child to be periodically reported on by the school doctor in the ordinary course of his visits to the school. Under this procedure the child is usually seen at intervals of about six months. In December, 1938, 2,632 children were thus being kept under observation.

(d) THE HOME ENVIRONMENT.—A report on the home conditions of each child admitted to a unit is obtained, a Care Committee worker visiting the child's home for this purpose. Should the report contain evidence of the presence of unsatisfactory conditions, the Borough Medical Officer of Health is informed. In 1938 1,744 such reports were sent in by Care Committee workers, and in 434 instances premises were reported to the local Medical Officers of Health for further investigation. The assistance of the Medical Officers of Health and the Care Committees is invaluable.

(e) CENTRAL CO-ORDINATION.—The responsibility of co-ordinating the various parts of the Rheumatism Scheme in London rests with the Supervising Medical Officer. He is responsible for:

(i) The control of the admissions of cases to the special rheumatism units.

(ii) Making arrangements for the supervision of children after they have been discharged from the units.

(iii) Deciding on the most suitable type of school for the child after its discharge from a unit.

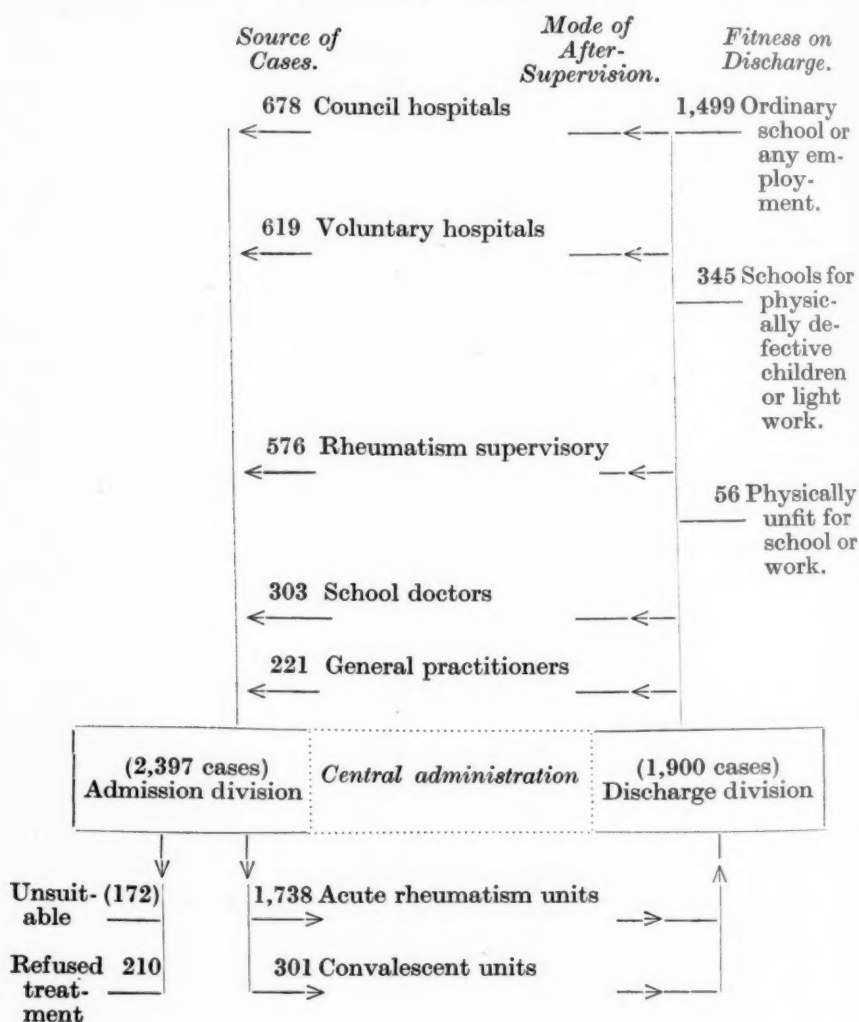
(iv) The general supervision of the work of the rheumatism supervisory centres.

(v) Effecting liaison between the medical officers doing work in connection with the various subdivisions of the scheme, and also between those working within the scheme, and others who, for one reason or another, may be interested in the children under treatment.

(vi) Supervision of registration and statistical work in connection with the scheme, and the preparation of an annual report.

RHEUMATISM SCHEME: DIAGRAMMATIC REPRESENTATION OF METHOD OF DEALING WITH RHEUMATIC CHILDREN REFERRED TO THE COUNCIL FOR INSTITUTIONAL TREATMENT UNDER THE SCHEME

(The figures refer to the number of children dealt with during 1936.)



CONTROL OF ADMISSIONS TO THE RHEUMATISM UNITS.—When application is made for the admission of a child to a rheumatism unit, the case is examined by a medical "referee." A detailed report and recommendation is prepared, and this is then used as a guide in the allocation of the case to the most suitable unit. A copy of this report is sent to the Medical Superintendent of the unit. In 1938, 2,230 such applications for treatment were received.

ARRANGEMENTS FOR SUPERVISION AFTER DISCHARGE FROM THE RHEUMATISM UNITS AND DECISION AS TO TYPE OF EDUCATION.—When a child is discharged, a report is sent to the Supervising Medical Officer giving details of the child's progress whilst in hospital and its condition on discharge. This report is considered, and a decision is made as to the type of school the child should attend. In case of doubt a special medical examination is arranged. A copy of the report is supplied to the doctor or hospital who originally nominated the child for treatment. Should the child be over school age, a report is sent to the After-Care Association indicating any special precautions which may be desirable, and advising as to a suitable type of work.

SUMMARY.—The London County Council's Rheumatism Scheme, which has been evolved for dealing with the problem of juvenile rheumatism and its sequelæ, is probably the most comprehensive of its kind in existence. It provides facilities for early diagnosis. It ensures that, for all cases needing it, an adequate period of institutional treatment is available. It includes arrangements for the education of the convalescent child whilst still in hospital, and for the constant medical supervision of every rheumatic child up to the age of leaving school. Nor does its influence then cease. With the collaboration of the After-Care Association for Blind, Deaf and Crippled Children (the latter class including "cardiac cripples") supervision continues, and work is found of a kind which can be safely undertaken by those suffering from the results of an attack of the disease.

TREATMENT

REST.—That rest is an essential factor in the treatment of acute rheumatism all are agreed, but there are differences of opinion as to the length of time this form of treatment should take and as to the best methods which can be employed to

obtain both rest for the body and rest for the mind. The older physicians were content to nurse their acute rheumatic patients in bed for a period of from three to six weeks, and then, if the temperature was normal, to allow them to resume their ordinary daily life, or to recommend a holiday or a short stay in a convalescent home, the entire course of treatment, including the convalescent period, taking three months or even less.

In the London County Council's hospitals rest under good hygienic conditions has been the mainstay of the treatment. Many of the rheumatic patients are at least six months in the hospital, and some of them stay for longer, the average period of stay in the acute and subacute units being just under seven months. The actual procedure is, of course, varied, according to the stage that the treatment has reached when the patient is admitted, and is also modified to some extent according to the progress and general clinical behaviour of the case, but as a rule every patient is nursed in bed for at least three months after admission. At first the child is kept flat, except for a pillow, and then by degrees allowed to sit up for strictly specified periods, which are gradually lengthened. Absolute recumbency is not entirely satisfactory, and at times defeats its own object. The rheumatic child, once the temperature has settled, feels perfectly well, and is often of a rather nervous and excitable disposition, and a prolonged period of forced recumbency proves a strain on the patient, and rest and strain are diametrically opposed. Rest must be natural, not forced, and the child must be at peace with its surroundings. Anything that can be done to keep the children happy and occupied without exerting them is of the greatest value and to be encouraged; nothing but harm is done by confining children to bed, and allowing them to become bored, dissatisfied and introspective.

At Queen Mary's Hospital, Carshalton, the treatment tends to follow these lines, though certain modifications have to be made for individual cases. If all has gone well with the rheumatic patients after being in bed for about three months, they are allowed up by degrees. At first they are allowed up for only an hour or two daily, and are not encouraged to take exercise; then this period is gradually lengthened and more freedom permitted; and, finally, when they are up for half a day or more they have exercises, games, dancing, etc., and are gradually brought to resume the normal activities of a healthy child.

The following are the points on which most stress is laid in assessing the progress of the case and deciding the rate at which progressive stages of the treatment can with safety be adopted. If there is a history that the patient has had a recent attack of what is undoubtedly rheumatism, and the heart is either undamaged or there is only a soft systolic murmur present at the apex, then a prolonged period of rest in bed is indicated. If the patient has had repeated rheumatic attacks and the heart is obviously enlarged and damaged, or if, as sometimes occurs, the heart has remained normal in spite of repeated attacks of rheumatism or chorea, then it would seem best to prolong the convalescent period of the treatment, and to reduce or to a large extent omit the period of absolute rest. The pulse is a valuable guide to the progress of the case. The pulse rate is recorded as a routine measure night and morning and at 2 p.m., and, if necessary, more frequently. If all has gone well during the period of rest the morning and evening pulse rates are about the same. When the patient begins to get up there is, as a rule, a slight rise, more especially of the evening pulse rate; but if the progress of the case has been satisfactory the rate should not be much over 100, and should tend to settle. It must, however, be remembered that there is a considerable degree of variation in the pulse rate of children, and in some cases a pulse rate of 120 or over goes with what appears to be a healthy heart; but as a rule a raised pulse rate, occurring as the result of the very gradual increase in activity that is allowed, must be taken as a danger signal. In cases where the pulse rate settles slowly or is easily raised it is considered best to retard the transfer to the convalescent wards. The temperature almost always settles very shortly after admission, and prolonged pyrexia is so rare that it is of little value as a guide in the general management of the treatment. The erythrocyte sedimentation test is also of value, a raised rate being almost always indicative of activity, if other infective conditions can be excluded. Unfortunately the test fails in cases of chorea. Nevertheless, in spite of these limitations, two years' experience of the routine use of the test at two of the units has afforded proof of its value in assessing the activity of the rheumatic infection.

EDUCATION.—The essential function of a rheumatism unit is of course to give the rheumatic child the prolonged treatment and nursing the disease requires, but ancillary to this is the

provision of facilities for education during the later stages of the treatment. If the children are to be kept at rest for any prolonged period, it is essential that they should be kept occupied, otherwise they become dull and irritable and the whole object of the treatment is frustrated. It is therefore a most valuable adjunct to treatment to have school work carried on in the wards, and the individuality of the teacher is a point of no mean importance. Moreover, a certain amount of suitably planned education provides that necessary mental background which enables the child to renounce gradually and naturally the rôle of invalid, and when discharged from hospital to re-enter the ordinary school world without any great or sudden change in its mode of life. Provision for education is therefore made in all the Council's rheumatism units which are recognised as "hospital schools" by the Board of Education. On the whole, the rheumatic children seem to be bright and eager, though all types of intellect are met with among them. They are, however, often backward owing to having lost time at school on account of ill-health. With suitable training they nearly all regain lost ground, and they certainly enjoy their lessons and feel something lost out of the day during the periods that are designated holidays. It seems advisable that there should be as few of these arbitrary breaks in the school work as possible. During the periods the patients spend in hospital they must, for various reasons, lose a certain number of school days, so that there is little danger of their being over-driven, and there seems little reason, so far as the children are concerned, why the formal holidays should be adhered to. It is only possible to carry out a limited amount of manual work, but towards the end of their stay in hospital a certain amount of simple handicraft is done, and all through the period most of the girls do knitting and needlework.

DIET.—The diet the rheumatic children receive is an ample but very simple one. It would seem that the hospital diet is much richer in both calcium and animal fats than that which most of them receive when in their own homes. Certain writers have commented upon the fact that rheumatic children tend to have a marked aversion to milk and a craving for strong-tasting acid types of food, such as vinegar, pickles and sauces. These idiosyncrasies are almost unknown in the rheumatism wards, and although occasionally there are children who do not care

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for milk, there have been few who would not take it, and so far as fads and peculiarities of diet are concerned, the rheumatic children seem to differ in no way from other patients. It must, of course, be remembered that very few of the rheumatic patients show clinical evidence of acute rheumatism for more than a week or two after admission, and it may be that it is while the disease is in the more active stage that the child tends to shun certain articles of diet. During the more acute stages of the disease rheumatic children tend to lose weight rapidly, but as soon as convalescence is reached they quickly regain this loss.

HELIO THERAPY.—During the summer months the rheumatic children are freely exposed to the natural sunlight, and just the customary precautions are taken to prevent actual sunburn or too prolonged exposure to the hot midday sun. Most of the patients pigment well, but their skin reactions seem to be very much as those of other patients. During the winter months artificial actinotherapy is employed, but only to a limited extent, as only those patients who are allowed to be out of bed can be treated. Carbon arc lamps are used, and at Queen Mary's Hospital, Carshalton, the child receives each week two or three light baths of about an hour's duration. It is very difficult to assess the value of light treatment. It would seem that its influence is not very marked, but on the whole it would appear to be beneficial and very pleasing to the children.

DRUGS.—Of the numerous drugs which have from time to time been tried, only the salicylates have remained persistently popular. Drugs of the sulphonamide group are now being given a trial, but it is yet too early to assess their value. Recently American authorities have published encouraging reports.

ARTIFICIAL PYREXIA.—Our experience of the results obtained by this method of treating chorea have been disappointing.

CLOTHING.—The view is very generally held that rheumatic children require rather special protection against the weather, and the advisability of wearing warm woollen underclothing and the danger of allowing rheumatic children to go about in shorts and other forms of dress that do not adequately protect the knees have been stressed by many writers. Also, it is the common teaching that rheumatic patients, when in bed, should be nursed between blankets. It would seem that there is very little foundation for these traditional beliefs. During the summer months the clothing of the rheumatic children is reduced to the very mini-

mum, and as a result of this they become very hardy and are in no hurry to resume their heavier clothing when in autumn the days become colder, and yet the recurrence of any rheumatic manifestations while the patients are in hospital is extremely rare. During the winter months the children are warmly clad, but many of the boys wear jerseys and shorts that leave the knees uncovered, and they seem to suffer in no way from this. The children are provided with overcoats, but, except on the very coldest days, they seem to prefer to be without them. Colds and intercurrent infections do occur, but they are not common, and as a rule the children throw them off easily, and so far as rheumatism is concerned relapses are very rare, and such vague conditions as "growing-pains" are almost unknown in the convalescent wards. Although all the rheumatic patients when first admitted are nursed in the wards, quite a large proportion of the convalescent cases sleep out under glass verandahs, even during the winter months. Also, unless the weather is very unsettled or it is actually raining, the beds are taken from the wards into the open courtyards daily during both summer and winter months. The result of all this fresh air and exposure seems to be highly beneficial.

In conclusion it may be said that rest under good hygienic conditions, with a very gradual return to the normal activities of life, is the basis of the treatment of juvenile rheumatic patients. The results are fairly successful, but the treatment has the inherent disadvantage of being lengthy and expensive, and has the obvious disadvantage of keeping children away from their homes for long periods. Any steps that could be taken to shorten the duration of the treatment or make more certain the immunity from relapses would be of the greatest value. Up to the present no specific treatment has been found.

TONSILLECTOMY.—The value of tonsillectomy as a method of preventing recurrences in cases of juvenile rheumatism or of warding off the cardiac complications has, in the past, been widely debated.

Very differing views are held by observers as to the part played by the tonsils in the ætiology and prognosis of rheumatic disease in children. Analyses in this connection are beset with difficulties. Unless very small numbers are considered (and this may result in deductions being vitiated by elementary statistical fallacies) there is always the possibility of errors being introduced

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owing to incomplete information in case notes "written up" by many different observers. Also, clinicians often differ considerably as to the standards they adopt in describing a tonsillectomy as "complete" and "satisfactory." Even more do differing standards influence case records when it is a matter of assessing whether cardiac damage is severe and progressive or slight and unimportant. These difficulties have not been absent in the analyses from which the figures tabulated below are derived.

Since bacteriological investigations had shown that hæmolytic streptococci were frequently present in the throats of children whose tonsils were chronically enlarged or inflamed, it was an obvious suggestion that removal of the tonsils should be a useful means of preventing the development of rheumatism in such children. The following analysis of cases treated under the London County Council's Rheumatism Scheme would seem to negative the soundness of this view:

RESULTS OF ANALYSIS OF 1,500 CASES OF JUVENILE RHEUMATISM ADMITTED TO THE COUNCIL'S RHEUMATISM UNITS WITH REFERENCE TO THE CONDITION OF THE TONSILS

Number in whom tonsils had been removed prior to first known attack	401
Number with unhealthy tonsils	307
Number with apparently healthy tonsils	744
Number removed between first and subsequent attacks	48
Total	1,500

Of significance also in this connection are the statistics relating to the number of tonsillectomies performed on London elementary school children. The number gradually rose from 7,656 in 1923 to 18,178 in 1931, and subsequently began to diminish. In fact, in 1931 the School Medical Officer estimated that one-third of London elementary school children had had their tonsils removed. Figures taken from the Annual Report of the Chief Medical Officer of the Board of Education indicate that about 50 per cent. of tonsillectomies are done on children between the ages of five and seven years inclusive. This period lies below the age of greatest incidence of juvenile rheumatism, and if the operation had any prophylactic value it would be reasonable to suppose that from 1931 onwards a sensible diminution in the incidence of juvenile rheumatism should be beginning to show itself; but there is no evidence of this, as the following figures show:

	1932.	1933.	1934.	1935.	1936.
Number of nominations for institutional treatment under the Council's scheme	1,234	1,845	1,571	1,703	1,719

(Note.—The 1935 and 1936 figures have been corrected to allow for certain administrative changes in the scheme.)

From the facts shown in the above tables it would seem to be reasonably certain that there is no statistical evidence pointing to the value of tonsillectomy as a means of preventing the occurrence of rheumatic infection, and one must conclude that if a hæmolytic streptococcus be the cause, unhealthy tonsillar or naso-pharyngeal lymphoid tissue is by no means a necessary factor in affording admission to the organism; nor does the removal of such tissue afford protection.

When, however, the severity of the attack was considered in conjunction with the condition of the tonsils, some interesting and suggestive figures were obtained. In considering the ætiology of juvenile rheumatism it was pointed out that in a series of 1,000 admissions to the rheumatism units in fifty-three instances the attack was preceded by a definite tonsillitis. An analysis of these figures showed that the general incidence of cardiac damage in the complete series amounted to 36 per cent., whereas in those cases where the attack was preceded by a tonsillitis the incidence of permanent cardiac damage was 70 per cent.

The subjoined tables also supply some interesting figures:

TABLE VII.—COMPARISON OF THE INCIDENCE OF THE MORE SEVERE AND PROGRESSIVE CARDIAC COMPLICATIONS IN RHEUMATIC CHILDREN WHOSE TONSILS HAVE BEEN REMOVED WITH THE INCIDENCE IN CHILDREN WHOSE TONSILS WERE IN SITU AT THE TIME OF THE FIRST ATTACK OF RHEUMATISM

(Figures from case records of children treated at Queen Mary's Hospital, Carshalton.)

Condition of Tonsillar Region.	Total Number.	Cardiac Condition.			
		Normal and Indefinite "Murmurs."		Mitral Stenosis, Mitral and/or Aortic Disease.	
		Number.	Percentage.	Number.	Percentage.
Tonsils not removed before onset ..	716	492	68.6	224	31.4
Tonsils satisfactorily removed before onset ..	159	123	77.3	36	22.7

It is seen that the children who had not had tonsillectomy performed showed an increase of 8.7 per cent. in the incidence of severe cardiac involvement as compared with the incidence in children who had had the operation.

A similar analysis was made of 1,500 cases admitted to the rheumatism units during the first half of 1937:

TABLE VIII

<i>Condition of Tonsillar Region.</i>	<i>Total Number.</i>	<i>Cardiac Condition.</i>			
		<i>Normal or Indefinite "Murmurs."</i>		<i>Mitral Stenosis, Mitral and/or Aortic Disease.</i>	
		<i>Number.</i>	<i>Per- centage.</i>	<i>Number.</i>	<i>Per- centage.</i>
Tonsils not re- moved before onset ..	1,099	828	75.4	271	24.6
Tonsils satisfactor- ily removed be- fore onset ..	401	325	81.1	76	18.9

In this table the difference between the percentage incidence of severe cardiac disease in the two groups is reduced to 5.7 per cent. as compared with the figures taken from the Queen Mary's Hospital records.

It is evident that the value of early tonsillectomy, with a view to preventing the occurrence of severe cardiac involvement, is a subject well worth further study, and the results of such an investigation might profoundly affect our conceptions as to the periods of institutional treatment required. Up to the present a very cautious attitude has prevailed in the matter of advising tonsillectomy, and the operation has been performed only when the tonsils were obviously grossly diseased and the rheumatic infection apparently quiescent. This conservative view may have to be modified as a result of further research.

The results of a Rheumatism Scheme must be chiefly judged by the measure of its success in reducing the incidence of the cardiac sequelæ of rheumatism, especially the incidence of permanent cardiac damage. In very few cases is a rheumatic attack unaccompanied by signs indicating the presence of a carditis. If, however, this can be induced to subside without permanent

valvular or myocardial damage no great harm is done. This, then, is the essential problem which has to be solved. With chronic and insidious diseases where no specific treatment is known it is always a difficult matter to prove that treatment on general lines is beneficial, and a true appreciation of its results can usually only be arrived at by a consideration of indirect evidence and by patient observation extending over many years. One method of assessing the results attained by the London County Council's Rheumatism Scheme is to ascertain if there has been any decrease in the incidence of rheumatic cardiac disease in London school children since the inception of the scheme. The figures given in the following table are suggestive:

TABLE IX.—PERCENTAGES OF ELEMENTARY SCHOOL CHILDREN FOUND BY SCHOOL DOCTORS TO BE SUFFERING FROM CARDIAC DISEASE

<i>Year.</i>	<i>Number of Children examined by School Doctors.</i>	<i>Number with Acquired Cardiac Disease.</i>	<i>Percentage.</i>
1923	236,658	5,011	2.1
1924	234,233	5,231	2.2
1925	281,595	5,952	2.1
1926	285,548	5,676	2.0
1927*	292,202	5,629	1.9
1928	304,206	5,872	1.9
1929	283,250	5,441	1.9
1930	253,656	4,667	1.8
1931	309,247	3,723	1.2
1932	315,880	3,868	1.2
1933	304,014	3,852	1.2
1934	297,801	3,845	1.3
1935	316,567	3,077	0.9
1936	301,392	2,648	0.8
1937	314,959	2,431	0.77

* Council's Rheumatism Scheme came into operation.

It will be noted a decrease of over 50 per cent. has occurred during the ten years the scheme has been in operation, and though it might be claiming too much to attribute the whole of this decrease to the effects of the scheme, it is not unreasonable to assume that it may claim some of the credit.

SUBSIDENCE OF CARDITIS.—In an analysis of 1,094 unselected cases discharged from the units in 1934, the fact was revealed that of the 600 who showed signs of cardiac involvement on admission, 149 (*i.e.*, nearly 25 per cent. of the number) had no signs of cardiac disease on discharge. Even allowing for the possibilities of observational variations the figures seem to afford striking evidence of the value of prolonged rest. Furthermore,

of the 494 cases without cardiac complications on admission, only ten developed signs of cardiac involvement whilst in hospital, and seven of these were of a very mild or doubtful type. There would certainly appear to be little risk of cardiac valvular disease developing if the child can be given complete rest in good surroundings at the onset of the disease.

ULTIMATE PROGNOSIS.—In order to arrive at some precise conclusion if possible as to the ultimate results in cases of juvenile rheumatism two groups, each consisting of 200 children, were studied. The first group consisted of children admitted to Queen Mary's Hospital during 1927. The second group was made up of children admitted in 1932. In the classification of the present condition of those still living, those who are now able to carry out their ordinary employment or attend their usual school have been classified as "alive and well," unless records show that they are carrying on their employment in spite of being crippled by heart disease. Those who are only fit to undertake light work or to receive education in a school for physically defective children, together with those who are known to be unfit for any form of occupation, have been classed under the heading "Invalided."

Unfortunately it was only possible to trace 242 of the 400 cases under review. An analysis of these cases was made in connection with the age of onset of the disease, and the results are summarised in the table given previously (Table I., p. 215). In the following table (Table X.) the 242 cases traced are classified according to the condition of the heart on admission, and the table summarises the ultimate outcome. As the numbers are only small, it was thought best to summarise the findings in a single table.

TABLE X.—CONDITION IN 1937 OF 240 RHEUMATIC CHILDREN GROUPED ACCORDING TO THE CARDIAC LESION PRESENT

<i>Condition of Heart on Admission.</i>	<i>Percentage Alive and Well.</i>	<i>Percentage of Invalids.</i>	<i>Percentage Deceased.</i>
No evidence of cardiac disease	80·0	17·5	2·5
Disease of mitral valve without stenosis	66·0	22·5	11·5
Disease of mitral valve with stenosis	37·7	27·5	34·8
Disease of aortic valve only	Only one case traced (alive and well)		
Disease of both mitral and aortic valves	9·0	9·0	82·0

From the preceding table it is seen that those admitted with extensive valvular lesions and evidence of mitral stenosis have, on the whole, done badly, and few of them can be classified as "alive and well." On the other hand, those that were admitted with no definite evidence of carditis or with only a systolic murmur in the mitral area have, with few exceptions, made a satisfactory recovery. Of the sixty-nine children showing signs of mitral stenosis who have been followed up, forty-three are either dead or invalided. On the other hand, sixty-two children with only slight mitral involvement have been traced, and of them forty-one are alive and well and only twenty-one dead or invalided.

SUMMARY AND SUGGESTIONS

(1) At the present time the immediate causation of juvenile rheumatism and the factors conducive to its occurrence are still imperfectly known, and until research is carried further no advance in the direction of prevention or treatment is probable.

(2) Following the more intensive supervision of school children during recent years, insidious rheumatism and carditis are discovered at an earlier stage, and admissions to the rheumatic units during the last three years have shown a distinctly milder type of cardiac involvement. The Rheumatism Supervisory Centres which have been established as part of the Council's Rheumatism Scheme carry out most essential work in this connection.

(3) During the eleven years which have elapsed since the inception of the Rheumatism Scheme a notable fall has occurred in the incidence of rheumatic heart disease in London school children.

(4) Up to the present time the treatment for juvenile rheumatism has been based on prolonged rest. It may be that further investigation of its ætiology will modify our views as to the length of time necessary for adequate treatment. If this period could be shortened it would be of much value in the matter of freeing beds for acute cases. In this connection studies should be made of the effect of early tonsillectomy on the prevention of the severer cardiac complications and of the influence of diet on the occurrence of juvenile rheumatism. A fuller investigation of the relationship of the disease to social conditions is also very

desirable, and an endeavour to elucidate the part played by hereditary influences might add much to our knowledge.

So far as drug treatment is concerned, no drug has yet been found which gives any better results than are obtained by the use of salicylates.

(5) It seems evident that more extensive provision for research on general questions relating to the incidence of juvenile rheumatism is urgently required, and that qualified research workers should be appointed for this purpose.

(6) The importance of careful selection of the medical and nursing staff cannot be overestimated. Doctors and nurses who show special aptitude for dealing with rheumatic cases should be encouraged and their services retained.

(7) Both from the point of view of the interests of the patients and the facilitation of research, cases should be transferred to special rheumatism units in the early acute stages of the disease. Too often, at present, are such patients retained in mixed general wards in town hospitals for considerable periods.

(8) It is a matter for regret that schemes for the treatment of juvenile rheumatism are at present applicable only to children under the age of sixteen. This precludes the supervision and treatment of many young adults. It also renders impossible the adequate following-up into adult life of the greater proportion of the juvenile cases. Advice in connection with suitable and unsuitable occupations, child-bearing, and general regimen is at present not readily accessible, and this fact is directly responsible for much chronic invalidism and reduced expectation of life. Supervisory clinics for young adults on similar lines to those available for children would be well worth their cost.

APPENDIX I

APPROXIMATE COST PER ANNUM OF TREATMENT AND SPECIAL EDUCATION OF RHEUMATIC CHILDREN IN LONDON

Annual cost of treatment and education of children in rheumatism units	£130,000
Annual cost of Rheumatism Supervisory Centres	1,850
Employment of consultants for special reports	900
Estimated extra cost of rheumatic children attending day schools for the physically defective	74,500
Total annual cost	207,250
Less contributions from relatives in respect of maintenance in the special hospitals	5,200
Net annual cost	£202,050

The London County Council is not called upon to find the whole of this amount, since, for children attending schools for the physically defective and for those under treatment in the rheumatism units which are recognised as hospital schools, the Council receives a grant from the Board of Education equal to 50 per cent. of the expenditure incurred.

APPENDIX II

PROVISION FOR THE TREATMENT AND SUPERVISION OF RHEUMATIC DISEASE IN LONDON CHILDREN APART FROM THAT MADE BY THE COUNCIL

(1) PROVISION BY VOLUNTARY HOSPITALS.—Large numbers of rheumatic children are treated annually both as in-patients and out-patients at the London voluntary hospitals. Figures relating to the number of rheumatic children treated as in-patients during 1936 were supplied through the courtesy of the respective secretaries of the following children's hospitals:

Belgrave Hospital	22 cases
Evelina Hospital	37 "
Hospital for Sick Children, Great Ormond Street	111 "
Paddington Green Children's Hospital	31 "
Princess Louise Hospital	59 "
Princess Elizabeth of York Hospital	104 "
Queen's Hospital for Children	66 "
Victoria Hospital for Children	37 "
Total	467 "

In addition, of course, many children are treated in voluntary hospitals not especially reserved for children.

(2) HEART HOMES AND HOSPITAL SCHOOLS OTHER THAN THE COUNCIL'S RHEUMATISM UNITS:

(a) Provided by the Invalid Children's Aid Association:						
West Wickham Heart Home	84 beds
Edgar Lee Home, Worthing	22 "
(b) Warren Heart Home, Lancing (Great Ormond Street Hospital)						
..	60 "
(c) St. John's (R.C.) Open Air School, Chigwell	42 "
(d) Cheyne Hospital, Chelsea (this, however, is chiefly for children from Surrey)						
..	25 "
Total	233 "

(3) BOROUGH RHEUMATISM SUPERVISORY CENTRES.—In the Royal Borough of Kensington and in the Borough of Paddington

Rheumatism Supervisory Centres have been established in connection with the public health services under the control of the respective Borough Medical Officers of Health.

(4) NOTIFICATION.—In London acute rheumatism is compulsorily notifiable in the following boroughs: Holborn, Paddington, the Royal Borough of Kensington.

For permission to use the material embodied in this paper the authors are indebted to Sir Frederick Menzies, K.B.E., M.D., F.R.C.P., F.R.S. (Edin.), Medical Officer of the London County Council.

In order to comply with the Standing Orders of the Council it is necessary to state that the Council accepts no responsibility for any opinion or conclusion expressed in this article.

ABSTRACTS FROM CURRENT LITERATURE

IS ARTICULAR RHEUMATISM AN ALLERGIC CONDITION? Herman Kirschhof. (From the Medical Clinic of the University of Munich.) *Zeitschrift für Rheumaforschung*, September, 1938, Band I., Heft 9, p. 302.

The author reviews the conclusions of many authorities upon this question and reports the results of experiments he has carried out to elucidate the problem. Aschoff, Gräff and Fahr think that articular rheumatism is a specific infection, though the exciting agent has not yet been discovered. In contrast with this view Klinge and Rössle think that the so-called fibrinoid degeneration is due to an allergic reaction. Rössle limits his opinion in this respect to acute articular rheumatism, whereas Klinge includes the chronic forms of arthritis, muscular rheumatism, gout and neuralgias. Klinge thinks that bacterial proteins are the allergic factor, but Gudzent considers they probably derive from decomposed foods and from proteins of animal and vegetable origin. These authors attach the term "visceral rheumatism" to many disorders of the heart, the pleura, the joints, arteries and veins. Kämmerer regards allergy as partly inborn, partly acquired specific reactivity to certain substances which are harmless to the normal person. Berger regards allergy as an antibody diathesis, using the term "diathesis" as a symptomless state in which the body is ready to react. An allergic disease may thus be regarded as an interaction between allergens and the antibody reaction. Gudzent bases his views on the results of skin tests; in 10 per cent. of non-rheumatic persons positive reactions occurred, and these he regards as due to a latent rheumatic state. The author has carried out experiments using allergenine, which is prepared from certain protein solutions. Out of 60 cases of acute and chronic arthritis, in 19 only was an unequivocal result obtained, and of these 11 gave negative results. He reports that his experiments have been repeated by others in 230 cases, with similar results. He also tested a series of patients suffering from diseases other than rheumatism, and out of 48 persons 39 gave positive results. He draws the conclusion on

grounds which are fully set out that there is no difference between the reactions of rheumatic cases and others. Experiments carried out to judge the value of skin tests showed that they diminished with age, though the general sensitivity might increase, and the conclusion was drawn that Gudzent's reactions are essentially physiological and resemble the phenomena of Storm van Leeuwen. Allergic conditions can often be identified best from the presence of eosinophilia, which was present in 11 to 17 per cent. of the author's cases.

The author draws the conclusion that Aschoff's view is supported by the high fever, the sedimentation rate, leucocytosis, frequent preceding sore throat and other infections, and the occasional benefit from tonsillectomy. Negative findings do not exclude the virus infections. He does not accept any generally allergic origin of acute or chronic rheumatic conditions.

C. W. B.

PREVENTION AND TREATMENT OF CATARRHAL RHEUMATISM.

Professor K. von Neergard (Zurich). *Zeitschrift für Rheumaforschung*, October, 1938, Band I., Heft 10.

The author contends that the great mass of the rheumatic infections are secondary or tertiary manifestations of invasion by the filtrable virus of the common cold, which was first identified by Kruse and named by him the aphanazon; further light has been thrown upon it by the experiments of Dochez and others. Without stressing the diagnostic differences between rheumatism of catarrhal origin and that due to coccal invasion, the author believes that the latter forms less than 10 per cent. of the whole. The effect of dealing with septic foci has, he thinks, been overstressed, and that many transient improvements after treatment of teeth or tonsils may be attributed to the non-specific stimulation of the operation.

Prophylactic measures should be directed to the raising of resistance. It is known that this quality is greater and more lasting if an acute infection has just passed; abortive attacks may even harm the patient, as for instance when, in the popular phrase, the cold "has not come out properly." It is suggested that the aim, therefore, ought not to be to diminish the severity of any catarrhal attack on this account. It appears likely that attendance at public functions and the numerous social contacts bring about an increase in chronic disease. Neufeld holds that the

repeated small infections arising from these are more lowering than occasional massive invasions.

The author advocates a policy of prophylaxis by measures directed to raising the resistance to such infections. The individual must be trained to changes of temperature by the application of alternate cold and heat to develop the reactive capacity of the body, but gradual and insidious chilling must be avoided. Such a hardening process may be carefully carried out in the open air. He advocates a popular campaign by means of pamphlets, etc., warning against damp houses, unsuitable food, bad teeth, etc. While advising open-air exercise, he warns against excessive sun-bathing. He condemns central heating and excessive sporting activity.

The views expressed in a long article frequently run counter to generally accepted ideas, but are worthy of careful consideration, especially by those interested in the social aspects of the rheumatism campaign.

C. W. B.

PATHOGENIC PLEUROPNEUMONIA-LIKE MICRO-ORGANISMS FROM ACUTE RHEUMATIC EXUDATES AND TISSUES. Homer F. Swift and T. McPherson Brown. *Science*, March 24, 1939, vol. lxxxix., p. 271.

This contribution strikes a new and hopeful note in the search for a specific infective agent in acute rheumatism. The work consisted of several stages. (1) Exudates from acute cases, after three to five passages on the chorio-allantoic membrane of the chick, have been found to produce characteristic lesions in it, described as structures surrounded by flattened epithelium, and containing in their centre condensed eosinophilic material and varying amounts of inflammatory reaction. The agent giving rise to these changes passes through a Berkefeld filter. (2) By inoculating mice intranasally with suspensions of these chick membranes, or with the filtrate, a pneumonic disease was induced that is also transmissible in series and filterable. (3) After a few subcultures in beef-serum-dextrose-broth, or on solid media rich in serum, pleuropneumonia-like organisms were grown alike from the affected chick membranes or from suspensions of the lungs of affected mice. (4) At this point an attempt was made to culture in the same way, and using the same repeated passage technique, rheumatic joint fluid and an excised erythema nodosum nodule, with the result that pleuropneumonia-like organisms were grown

from both. These cultures were then found to produce in mice the same type of pneumonia that had been produced by infecting them with the chick membrane cultures. Thus, it was possible to cultivate on cell-free media pleuropneumonia-like organisms from exudates of patients with rheumatic fever, from chick membranes inoculated therewith, and from the lungs of mice inoculated with either. This success seems to have been due chiefly to the repeated passage technique alike in the animals and in the media used. Further reports of this new and promising work will be awaited with interest. Although the authors rightly decline to pronounce on the ætiological significance of their results at the present stage, it would seem likely that the question of the presence of specific antibody in the serum of patients may be helpful on that matter.

M. H. G.

EMPIRE RHEUMATISM COUNCIL

PROGRESS REPORT BY THE ORGANISING SECRETARY

THE period since October, 1938, has been marked by considerable progress in the Empire Rheumatism Council's "War on Rheumatism." Some of the more important developments are here noted.

At the request of the International League against Rheumatism, the Scientific Advisory Committee of the Empire Rheumatism Council has taken the responsibility of appointing the National Committee to represent the League in Great Britain. This National Committee has been constituted as follows: F. J. Bach, D.M.; C. W. Buckley, M.D., F.R.C.P.; W. S. C. Copeman, M.D., F.R.C.P.; A. G. Timbrell Fisher, M.C., F.R.C.S.; R. Fortescue Fox, M.D., F.R.C.P.; G. Holmes, M.B.; G. D. Kersley, M.D., M.R.C.P.; B. Schlesinger, M.D., F.R.C.P.; Sir William Willcox, K.C.I.E., M.D., F.R.C.P.; Sir Robert Stanton Woods, M.D., F.R.C.P.

The work of the Research Advisory Committee is progressing well. There are at present three semi-permanent Research Foundations (for periods of from three to seven years). Each of these, apart from the work in its own laboratory, has helpful association with, and the active collaboration of, other research institutions at Universities and Hospitals. The number of additional research efforts financed by the Empire Rheumatism Council in various Universities or other institutions is now eight.

The work of the Research Foundation to investigate the incidence of Rheumatic Disease in the training establishments of the Royal Navy, in which the Admiralty Medical Services are co-operating with the Empire Rheumatism Council, is developing most favourably. A special Sub-Committee of the Research Advisory Committee (with co-opted members) has been constituted to supervise the work of this Foundation, as follows: Lord Horder, G.C.V.O., F.R.C.P.; W. S. C. Copeman, M.D., F.R.C.P.; Mervyn H. Gordon, C.M.G., F.R.S., D.M.; Professor Geoffrey Hadfield, M.D., F.R.C.P.; Professor T. J. Mackie, M.D.; Professor J. W. McNee, D.S.O., M.D., F.R.C.P.; Mr. Frederick F. A. Pearson; Dr. Bernard Halley Stewart, F.R.S.E.; Sir William Willcox, K.C.I.E., F.R.C.P. (Chairman).

The sub-committee has authorised Dr. C. A. Green to visit the U.S.A. to study the work of Dr. Homer Swift in investigating a virus infection as a causative factor in Rheumatic Disease.

Investigation of the successful results obtained at Warsaw University of a serological test for rheumatic infection is proceeding actively under the charge of Dr. Mervyn Gordon. The co-operation of the L.C.C. Medical Services, of Edinburgh University, of Dundee University and of St. Bartholomew's Hospital, has been enlisted. The latest reports from Warsaw state that the test has now been applied in 1,000 cases of rheumatism, and in numerous control cases, and the results continue to be highly specific.

The Chemical Sub-Committee of the Scientific Advisory Committee has instituted an investigation of gold therapy in rheumatoid arthritis, with a carefully planned system of controls and provision for independent assessment of clinical results and of statistical check. This sub-committee consists of: F. J. Bach, D.M.; W. S. C. Copeman, M.D., F.R.C.P.; Professor L. S. P. Davidson, M.D., F.R.C.P., F.R.S.E.; Professor F. R. Fraser, M.D., F.R.C.P.; S. J. Hartfall, M.D.; Professor J. W. McNee, D.S.O., M.D., F.R.C.P.; W. S. Tegner, M.R.C.P.; E. C. Warner, M.D., F.R.C.P.; Lionel Whitby, C.V.O., M.D., F.R.C.P.; Sir William Willcox, K.C.I.E., F.R.C.P.

The propaganda work of the Council is progressing well, in spite of the preoccupation of the public mind with urgent questions of national defence. Total circulation of various educational pamphlets by the Council now approaches 25,000 copies; total attendances at educational meetings promoted about 4,000; total of Press articles regarding its work about 2,000—representing probably about 5,000,000 readers. It will be seen that the attention given by the Press is far the most important part of the Council's propaganda work.

It has been intimated to the Council by the Gas Light and Coke Company that, in a forthcoming educational film published by them, special attention will be given to the work of the Empire Rheumatism Council.

At the Annual Meeting of the Association of Approved Societies, London, June 9 and 10, Mr. E. G. Bearn, C.B.E., Deputy Controller Insurance Department, Ministry of Health, referring to Rheumatic Disease noted that "the Empire Rheumatism Council was energetically pursuing the study of this most deadly of all diseases."

The Annual Report, 1938, of the Joint Committee of Approved Societies devotes much attention to Rheumatic Disease; and urges the Approved Societies "to support the Empire Rheumatism Council to the limit of their powers." It calls attention to the fact that Approved Benefit 16 can only be applied to a very limited number of Rheumatism Clinics, and notes: "Approved Societies which have a widely distributed membership have begun to view with some concern the continued inclusion of a benefit in their schemes which, contrary

to all other additional treatment benefits, is necessarily restricted to those members who reside sufficiently near to the approved clinics to be able to attend as out-patients. A remedy for this would be the approval by the Department of other institutions and this, it is hoped, will shortly be announced."

The Conference of Trade Union Approved Societies at Scarborough (June) devoted much attention to Rheumatic Disease. The Presidential Address by Mr. G. W. Canter, after noting the voluntary work of the Empire Rheumatism Council, expressed strongly the view "that it is the duty of the State to undertake this work, no matter what the cost may be, until this curse has been successfully eradicated from our midst."

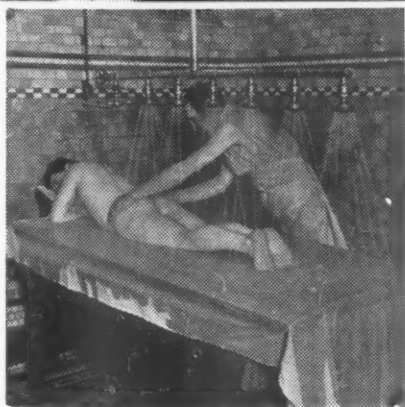
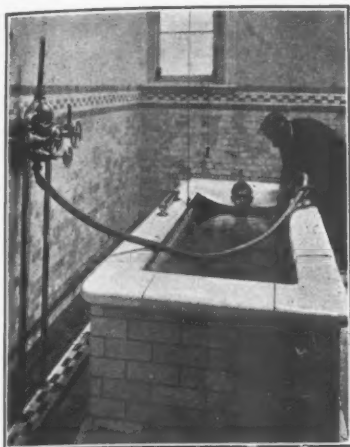
The Royal Institute of Public Health and Hygiene at its Annual Congress at Hastings, May 23-27, included a Section, "Rheumatism and Allied Diseases," for the organisation of which the Empire Rheumatism Council was invited to take responsibility.

Sir Frank Fox, O.B.E., was the President of the Section and took as the subject of his address "Industry and Rheumatism." There followed on the first day papers by Sir Morton Smart, K.C.V.O., M.D., on "Physical Medicine and Industry," and by Dr. G. C. Pether of the Devonshire Royal Hospital, Buxton, on "The Influence of Industry on the Development of Rheumatism."

The second day was given up to a discussion of the responsibility which various authorities could appropriately take in the war on Rheumatism. The subject was introduced by Capt. G. S. Elliston, M.C., M.P.; James Fenton, C.B.E., M.D.; and Professor L. S. P. Davidson, M.D., F.R.C.P.E., F.R.S.E.

On the third day there were papers by H. G. McGregor, M.D.; W. H. Bradley, D.M.; and H. A. Burt, M.B.; Dr. W. S. C. Copeman, Medical Secretary Empire Rheumatism Council, attended the Congress and arranged interesting and useful private conferences on Rheumatic Diseases, supplementary to the official proceedings.

The chronic rheumatic diseases, resistive to ordinary methods, yield to spa treatment.



For example, in cases of fibrositis and chronic arthritis spa methods secure :

- (i) Elimination of toxins *by internal and external application of the mineral waters.*
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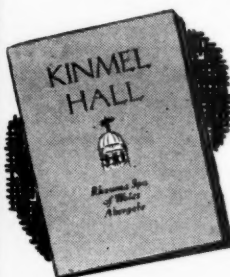
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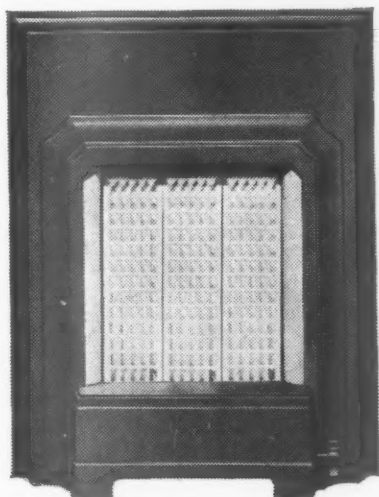
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THE SCIENTIFIC ADVISORY COMMITTEE, EMPIRE RHEUMATISM COUNCIL

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